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Evaluation Report

Spinetoram (XDE-175)

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Overview

Registration Decision for Spinetoram

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for Spinetoram Technical Insecticide, Radiant SC Insecticide and Delegate WG Insecticide containing the technical grade active ingredient spinetoram to control a variety of insect pests in pome fruits, asparagus, bushberries, cereals, caneberries, cole crops, fruiting vegetables, grape, leafy vegetables, root vegetables, stone fruits, soybeans and strawberries.

Current scientific data from the applicant were evaluated to determine if, under the proposed conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This report summarizes the information that was evaluated and provides the results of the evaluation as well as the reasons for the registration decision, with an outline of the additional scientific information required from the applicant. It also describes the conditions of registration that the applicant must meet to ensure that the health and environmental risks as well as the value of these pest control products are acceptable for their intended use.

This Overview describes the key points of the evaluation, while the Science Evaluation section provides detailed technical information on the human health, environmental and value assessments of Spinetoram Technical Insecticide, Radiant SC Insecticide and Delegate WG Insecticide.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by Subsection 2(1) of the *Pest Control Products Act* "...the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (a) efficacy; (b) effect on host organisms in connection with which it is intended to be used; and (c) health, safety and environmental benefits and social and economic impact".

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (e.g. children) as well as organisms in the environment (e.g. those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties present when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk reduction programs, please visit the PMRA's website at www.pmra-arla.gc.ca.

What is Spinetoram?

Spinetoram is a non-systemic insecticide derived from the fermentation of *Saccharpolyspora spinosa*. The end-use products Radiant SC and Delegate WG Insecticides are applied using ground application equipment to control a variety of insect pests on a wide range of fruit, vegetable and cereal crops. Spinetoram affects insects through both contact and ingestion, but is most active through ingestion.

Health Considerations

Can Approved Uses of Spinetoram Affect Human Health?

Spinetoram is unlikely to affect your health when used according to the label directions.

Exposure to spinetoram may occur through diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. Toxicology studies from another technical grade active ingredient, Spinosad (REG2001-10), of almost identical structure (derived from the same soil bacteria) and toxicological properties, were also considered in assessing the potential hazards to health associated with spinetoram.

The technical grade active ingredient spinetoram is a potential skin sensitizer. Consequently, the statement "Potential Dermal Sensitizer" is required on the label. Spinetoram was not genotoxic and is not expected to cause cancer in animals. There was also no indication that spinetoram caused damage to the nervous system. The first signs of toxicity in animals given daily doses of spinetoram over longer periods of time were effects on the thyroid gland, lymphoid tissues, kidneys, spleen and blood system. When spinetoram was given to pregnant animals, there were no effects on the developing fetus,

indicating that the fetus was not more sensitive to spinetoram than the adult animal. However, mothers had difficulty delivering their young in the reproduction study. The health effects noted in animals occur at doses more than 100-times higher (and often much higher) than levels to which humans are normally exposed when using spinetoram products according to label directions.

The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

Residues in Water and Food

Dietary risks from food and water are not of concern

Aggregate dietary intake estimates (food plus water) revealed that the general population and children 1–2 years old, the subpopulation which would ingest the most spinetoram relative to body weight, are expected to be exposed to less than 67% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from spinetoram is not of concern for all population sub-groups. Spinetoram is not carcinogenic, therefore a chronic cancer dietary risk assessment is not required.

Animal studies revealed no acute health effects. Consequently, a single dose of spinetoram is not likely to cause acute health effects in the general population (including infants and children).

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted in Canada and side-by-side trials conducted in the United States using spinetoram and spinosad on apple, sugar beet, leafy lettuce, orange, tomato and grass forage were acceptable. The MRLs for spinetoram can be found in the Science Evaluation of this Evaluation Report.

Occupational Risks From Handling Radiant SC Insecticide or Delegate WG Insecticide

Occupational risks are not of concern when Radiant SC Insecticide and Delegate WG Insecticide are used according to the proposed label directions, which include protective measures.

The label will specify that anyone mixing or loading Radiant SC Insecticide or Delegate WG Insecticide or performing clean-up or repair activities must wear coveralls over long-sleeved shirt and long pants, shoes plus socks and chemical-resistant gloves.

Workers applying either product must wear long-sleeved shirt and long pants, shoes and socks and chemical-resistant gloves. Taking into consideration these label requirements, risk to workers handling Radiant SC Insecticide or Delegate WG Insecticide is not of concern.

Environmental Considerations

What Happens When Spinetoram is Introduced Into the Environment?

Spinetoram rapidly transforms in the terrestrial and aquatic environment. The parent compound and its major transformation product, N-demethyl-J, are non-persistent in the environment and have a low potential for residue carryover. They also have a low potential to leach and contaminate groundwater. Based on its low volatility, spinetoram residues are not expected in the air.

Spinetoram presents a low risk to wild birds, earthworms, freshwater and marine fish, marine invertebrates, algae and aquatic plants. The proposed use of spinetoram will, however, pose an acute risk to bees, dietary risk to wild mammals, adverse effects on terrestrial plants and chronic risk to fresh water invertebrates and benthic organisms. It may also have toxic/adverse effects on beneficial predatory and parasitic arthropods. Mitigatory measures such as buffer zones and environmental hazard/precautionary label statements are required to protect these organisms.

Value Considerations

What is the Value of Spinetoram?

Spinetoram is an insecticide that controls or suppresses a variety of insect pests of fruit, vegetable and cereal crops.

Application of spinetoram provides effective control or suppression of a variety of insect pests of fruit, vegetable and cereal crops. It is also compatible with current management practices and conventional crop production systems. Growers are familiar with the monitoring techniques to determine if and when applications are needed.

One other active ingredient in the same chemical class as spinetoram is currently registered for some of the same uses; however, spinetoram is registered for use against a broader range of pests. Prudent use of these insecticides should be observed to prevent the development of resistance.

Measures to Minimize Risk

Labels of registered pesticide product include specific instructions for use. Directions include risk reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk reduction measures required on the label of spinetoram to address the potential risks identified in this assessment are as follows:

Key Risk-Reduction Measures

- **Human Health**

    - Anyone mixing or loading Radiant SC Insecticide or Delegate WG Insecticide or performing clean-up or repair activities must wear coveralls over long-sleeved shirt and long pants, shoes plus socks and chemical-resistant gloves. Workers applying either product must wear long-sleeved shirt and long pants, shoes plus socks and chemical-resistant gloves.

    - Label restriction to limit rotational crops to labelled crops only.

- **Environment**

    Risk to bees, predatory and parasitic arthropods and wild mammals is mitigated by the appropriate label statements. Risk to terrestrial organisms, freshwater invertebrates and benthic organisms is mitigated by environmental hazard statements and buffer zones.

What Additional Scientific Information is Being Requested?

Although the risks and value have been found acceptable when all risk reduction measures are followed, the applicant must submit additional scientific information as a condition of registration. More details are presented in the Science Evaluation section of this Evaluation Report or in the Section 12 Notice associated with these conditional registrations. The applicant must submit the following information by 1 September 2010.

- **Chemistry**

    The following studies are required to complete the chemistry database for these products:

    - Analytical data from at least five batches of technical grade active ingredient representing full-scale production and a revised statement of product specification form (SPSF) are required. Validated analytical methods and confirmation of identity must be provided for all impurities.

- Storage stability data for both end-use products representing at least one year of storage at ambient conditions are required.

- **Human Health**

  The following studies are required for the toxicity database for spinetoram:

  - 90-day Inhalation study
  - Information identifying the contents of the vacuoles (histochemical analysis) observed in various tissues of lymphoid and endocrine systems; this requirement may be satisfied concurrently with the 90-day inhalation study
  - 2-year chronic toxicity/carcinogenicity study in rats

  The following studies are required for the food residue database for spinetoram.

  - Processing studies on orange and grape.

- **Environment**

  The following studies are required:

  - acute toxicity to *Daphnia* sp (DACO 9.3.2)
  - acute toxicity to cold water fish (DACO 9.5.2.1)

  - The modified soil and sediment analytical method which includes the O-demethyl-175-J and O-demethyl-175-L metabolites.

Other Information

As these conditional registrations relate to a decision on which the public must be consulted[3], the PMRA will publish a consultation document when there is a proposed decision on applications to convert the conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

The test data cited in this Evaluation Report (i.e. the test data relevant in supporting the registration decision) will be made available for public inspection when the decision is made to convert the conditional registrations to full registrations or to renew the conditional registrations (following public consultation). If more information is required, please contact the PMRA's Pest Management Information Service by phone (1-800-267-6315) or by e-mail (pmra_infoserv@hc-sc.gc.ca).

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[3] As per subsection 28(1) of the *Pest Control Products Act*.

Science Evaluation

Spinetoram

1.0 The Active Ingredient, Its Properties and Uses

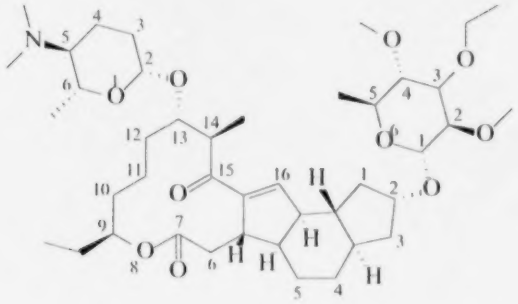
Spinetoram is comprised of two factors, XDE-175-J and XDE-175-L (3:1, J:L).

1.1 Identity of the Active Ingredient

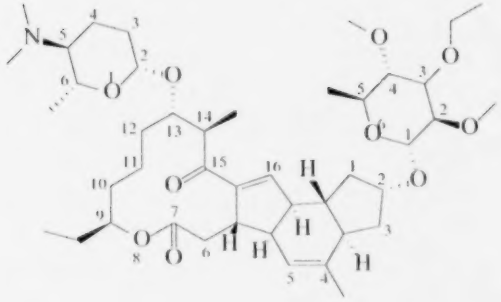
Active substance	Spinetoram
Function	Insecticide
Chemical name	
1. **International Union of Pure and Applied Chemistry (IUPAC)**	XDE-175-J (2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*)-13-{[(2*R*,5*S*,6*R*)-5-(dimethylamino)-6-methyltetrahydro-2*H*-pyran-2-yl]oxy}-9-ethyl-14-methyl-7,15-dioxo-2,3,3a,4,5,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-octadecahydro-1*H*-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranoside XDE-175-L (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)-13-{[(2*R*,5*S*,6*R*)-5-(dimethylamino)-6-methyltetrahydro-2*H*-pyran-2-yl]oxy}-9-ethyl-4,14-dimethyl-7,15-dioxo-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-1*H*-as-indaceno[3,2-d]oxacyclododecin-2-yl 6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranoside
2. **Chemical Abstracts Service (CAS)**	XDE-175-J 1*H*-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro-14-methyl-, (2*R*,3a*R*,5a*R*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*R*) XDE-175-L 1*H*-as-Indaceno[3,2-d]oxacyclododecin-7,15-dione, 2-[(6-deoxy-3-*O*-ethyl-2,4-di-*O*-methyl-α-L-mannopyranosyl)oxy]-13-[[(2*R*,5*S*,6*R*)-5-(dimethylamino)tetrahydro-6-methyl-2*H*-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-, (2*S*,3a*R*,5a*S*,5b*S*,9*S*,13*S*,14*R*,16a*S*,16b*S*)

CAS number	XDE-175-J:	187166-40-1
	XDE-175-L:	187166-15-0
Molecular formula	XDE-175-J:	$C_{42}H_{69}NO_{10}$
	XDE-175-L:	$C_{43}H_{69}NO_{10}$
Molecular weight	XDE-175-J:	748.0
	XDE-175-L:	760.0

Structural formula XDE-175-J



XDE-175-L



Purity of the active ingredient XDE-175-J plus XDE-175-L 86.4 % nominal (limits: 81.2%–91.6%)

1.2 Physical and Chemical Properties of the Active Ingredients and End-Use Product

Technical Product—Spinetoram Technical Insecticide

Property	Result
Colour and physical state	Off-white solid
Odour	Musty odour
Melting range	Compound (purity) — Temp °C XDE-175-J (99.0%) — 143.4 XDE-175-L (99.1%) — 70.8
Boiling point or range	Compound (purity) — Temp °C XDE-175-J (99.0%) — Decomposes at 297.8°C before boiling XDE-175-L (99.1%) — Decomposes at 290.7°C before boiling
Density	Relative density — 1.1485 g/cm^3 at 20°C Bulk density — 0.24 g/cm^3 at 22.8°C
Vapour pressure	Compound (purity) — Vapour pressure XDE-175-J (99.0%) — 5.3×10^{-5} Pa at 20°C 6.0×10^{-5} Pa at 25°C XDE-175-L (99.1%) — 2.1×10^{-5} Pa at 20°C 4.2×10^{-5} Pa at 25°C
Henry's law constant at 20°C	XDE-175-J — 3.913×10^{-8} atm m^3/ mole 1/H: 6.143×10^5 XDE-175-L — 4.938×10^{-8} atm m^3/ mole 1/H: 4.868×10^6

Property	Result			
Ultraviolet (UV)-visible spectrum	Compound (purity)	Solution	Wavelength λ_{max}, nm	Extinction coefficient ε, L/(mol·cm)
	XDE-175-J (97.6%)	Neutral	245	12 200
		Basic (pH 12.6)	246	11 700
		Acidic (pH 1.04)	247	12 400
	XDE-175-L (96.1%)	Neutral	243	11 100
		Basic (pH 12.6)	244	11 200
		Acidic (pH 1.04)	202 245	9800 11 400
Solubility in water at 20°C	Compound (purity)	Solution	Solubility (mg/L)	
	XDE-175-J (99.0%)	Purified water	10.0	
		pH 5 buffer	423	
		pH 7 buffer	11.3	
		pH 9 buffer	8.0	
		pH 10 buffer	6.27	
	XDE-175-L (99.1%)	Purified water	31.9	
		pH 5 buffer	1.63 g/L	
		pH 7 buffer	46.7	
		pH 9 buffer	1.98	
		pH 10 buffer	0.706	
Solubility in organic solvents at 20°C	Solvent	Solubility (g/L)		
	Methanol	> 250		
	Acetone	> 250		
	Xylene	> 250		
	1,2-Dichloroethane	> 250		
	Ethyl acetate	> 250		
	Heptane	61.0		
	n-Octanol	132.0		
n-Octanol–water partition coefficient (K_{ow})	Compound (purity)	pH	log K_{ow}	
	XDE-175-J (99.0%)	5	2.44	
		7	4.09	
		9	4.22	
	XDE-175-L (99.1%)	5	2.94	
		7	4.49	
		9	4.82	

Property	Result
Dissociation constant (pK_a)	Compound (purity) — pK_a XDE-175-J (99.0%) — 7.86 XDE-175-L (99.1%) — 7.59
Stability (temperature, metal)	Stable to heat, metals and metal ions. Slight degradation of the test substance was noted in the presence of $FeCl_3 \cdot 6H_2O$.

End-Use Products—Radiant SC Insecticide (GF-1587 SC Insecticide) and Delegate WG Insecticide (GF-1640 WG Insecticide)

Property	Radiant SC Insecticide	Delegate WG Insecticide
Colour	Gray	Tan
Odour	Musty odour	Musty odour
Physical state	Liquid	Solid
Formulation type	Suspension	Wettable granules
Guarantee	Spinetoram - 120 g/L nominal (limits: 114 g/L–126 g/L)	Spinetoram - 25% nominal (limits: 24%–26%)
Container material and description	1 L and 4 L, high density polyethylene (HDPE) jugs	1 kg, 1.7 kg and 2 kg foil/laminate bags
Density	1.0319 g/mL at 20°C	0.4–0.6 g/mL
pH	7.15 for 1% w/w dilution in distilled water at 22.7°C	8.66 for 1% dilution in distilled water at 22.6°C
Oxidizing or reducing action	The product does not contain any oxidizing or reducing agents.	The product does not contain any oxidizing or reducing agents.
Storage stability	An interim report showed the product to be stable when stored for 8 weeks at 40°C in polyethylene terephthalate (PET) and high density polyethylene (HDPE) bottles.	An interim report showed a decrease of 3% in active concentration after 2 weeks storage at 54°C in glass container.
Explodability	Not explosive	Not explosive

1.3 Directions for Use

The active ingredient, spinetoram, is formulated into two Commercial class end-use products, Radiant SC Insecticide and Delegate WG Insecticide. These products may be applied using conventional ground application equipment at application rates and re-application intervals that vary depending on the pest and crop (Table 1.3.1). Both products are registered for the same uses and the same application rate of active ingredient per hectare for any given use. All uses are limited to a maximum of three applications per year.

Table 1.3.1 Application Rates and Re-application Intervals for Radiant SC Insecticide and Delegate WG Insecticide

Pest(s)	Crop(s)	Application Rate (g a.i./ha)	Re-application Interval
Apple Maggot (suppression)	Pome Fruit	105	14 days
Armyworm	Cereals Soybean	25–50	5 days
Asparagus Beetle (suppression)	Asparagus (ferns only)	35–70	5 days
Blueberry Spanworm (suppression)	Bushberries	25–50	6 days
Cabbage Looper	Fruiting Vegetables and Okra Leafy Vegetables (non-*Brassica*)	35–50	5 days
Cabbage Looper Imported Cabbageworm Diamondback Moth	Cole Crops (*Brassica* Leafy Vegetables) Leaves of Root and Tuber Vegetables Root Vegetables	35–50	5 days
Codling Moth	Pome Fruit	105	14 days
Grape Berry Moth (suppression)	Grape	70	5 days
Obliquebanded Leafroller	Caneberries	25–50	5 days

Pest(s)	Crop(s)	Application Rate (g a.i./ha)	Re-application Interval
Obliquebanded and Threelined (Pandemis) Leafrollers	Pome Fruit Stone Fruit	53–105	14 days
Oriental Fruit Moth	Pome Fruit Stone Fruit	105	14 days
Plum Curculio (suppression)	Pome Fruit	105	14 days
Spotted and Western Tentiform Leafminers	Pome Fruit	53–105	7 days
Thrips (suppression)	Strawberry	50–70	3 days

1.4 Mode of Action

Spinetoram is classified as a Group 5 Insecticide, an acetylcholine receptor modulator (Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*). Spinetoram causes persistent activation of nicotinic acetylcholine receptors via an allosteric mechanism, thus disrupting normal synaptic signal transmission in the insect central nervous system. This particular mode of action is unique to spinetoram and the related active ingredient spinosad, which is the only other Group 5 Insecticide currently registered in Canada.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The analytical method provided for the analysis of the active ingredient in Spinetoram Technical Insecticide has been validated and assessed to be acceptable for the determination of both active factors in the technical material.

Impurity analyses were conducted using rudimentary methods (non-validated) since standards were not available for most impurities and with the understanding that the impurity profile will be variable between pilot/lab scale and full scale production. The full batch characterization will be conducted using validated methods once full scale production begins.

2.2 Method for Formulation Analysis

The methods provided for the analysis of the active ingredient in both formulations have been validated and assessed to be acceptable for use as enforcement analytical methods.

2.3 Methods for Residue Analysis

High-performance liquid chromatography methods with tandem mass spectrometry (HPLC-MS/MS) were developed and proposed for data generation and enforcement purposes. These methods fulfilled the requirements with regards to selectivity, accuracy and precision at the respective method limit of quantitation. Acceptable recoveries (70–120%) were obtained in environmental media and plant and animal matrices. Adequate extraction efficiencies in plant and animal matrices were demonstrated using radiolabelled apple, lettuce and goat liver samples analyzed with the enforcement method. Methods for residue analysis are summarized in Appendix I, Table 1.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

The PMRA has performed a hazard characterization of spinetoram. Spinetoram is derived from the same soil bacteria as another currently registered pesticide active ingredient, spinosad. The two compounds are almost structurally identical. They differ in that spinetoram is comprised of factors J and L (3:1), while spinosad is composed of factors A and D (7:1). The full array of toxicology studies currently required for hazard assessment is available for spinosad (See REG2001-10).

A request by the applicant to bridge the requirements for several core toxicology studies to the spinosad database, pending the completion of comparable studies with spinetoram, was accepted in principle by the PMRA. This acceptance was based on an initial assessment showing a similar toxicity profile when comparable toxicology studies with both chemicals were examined. The current assessment takes into account knowledge of the spinosad toxicology database to supplement the findings in the spinetoram database and, as required, for the purpose of selection of reference doses/toxicology endpoints for risk assessment.

With the exception of a 2-year rat study, the spinetoram database consists of the full array of laboratory animal (in vivo) and cell culture (in vitro) toxicity studies currently required for health hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practice. The scientific quality of the data is high and the database is considered adequate to characterize the toxicity of this pest control product. Where appropriate, reference is made to spinosad toxicology data in the following discussion of the toxicology profile of spinetoram.

Technical spinetoram was of low acute toxicity by the oral, dermal and inhalation routes in rats. It was non-irritating when applied to the skin and eyes of rabbits. Results of skin sensitization testing in mice using the Local Lymph Node Assay were positive.

Spinetoram insecticide formulation Radiant SC Insecticide was of low acute toxicity by the oral, dermal and inhalation routes in rats. It was minimally irritating when applied to the skin and eyes of rabbits. Results of skin sensitization testing in mice using the Local Lymph Node Assay were negative.

Spinetoram insecticide formulation Delegate WG Insecticide was of low acute toxicity by the oral, dermal and inhalation routes in rats. It was non-irritating when applied to the skin and minimally irritating to the eyes of rabbits. Results of skin sensitization testing in mice using the Local Lymph Node Assay were negative.

Spinetoram is comprised of two analogs (XDE-175- J and XDE-175-L) in a ratio of approximately 3:1 (J:L). Absorption and excretion of single or repeated oral doses or single i.v. doses of XDE-175-J or XDE-175-L was very rapid. A minimum of 70% of the administered dose was absorbed, and excretion was extensive, with feces as the principal route of clearance for both analogs. Within 168 hours, more than 88% of the administered dose for both analogs was detected in the urine and feces. For XDE-175-J, the highest levels of tissue residues occurred in the fat, kidneys, liver and lymph nodes, and the ovaries in females. For XDE-175-L, the highest levels were found in fat, lymph nodes, skin and adrenals in males, and fat, ovaries, lymph nodes, uterus, skin and adrenals in females.

Several metabolites were isolated, identified and characterized from urine and feces of rats treated with radiolabelled spinetoram. Spinetoram was almost completely metabolized by glutathione conjugation of the XDE-175-J parent compound, as well as glutathione conjugation with *N*-demethylated, *O*-deethylated and hydroxylated forms of the XDE-175-J parent compound, in conjunction with glutathione conjugation of the XDE-175-L parent compound, as well as glutathione conjugation with *N*-demethylated and *O*-deethylated forms of the XDE-175-L parent compound. No quantitative sex differences were observed. There were seven major metabolites identified after XDE-175-J administration and nine identified after XDE-175-L administration. The total administered dose accounted for in the excreta was 86.4–94.7 % of XDE-175-J and 82.0-89.1% of XDE-175-L.

A short-term dermal toxicity study showed non-adverse treatment-related skin irritation in all of the test groups after repeated applications of spinetoram to the shaved skin of rats. No signs of systemic toxicity were observed up to and including the highest dose tested (1000 mg/kg bw/day).

Generalized toxicity was observed in rats, mice and dogs as slight decreases in body weight, body-weight gain and/or food consumption following repeated dosing. Various blood parameters were also affected at higher doses throughout the spinetoram database. Hypochromasia and/or polychromasia of the erythrocytes was observed in dogs. Hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, red blood cells and/or platelets were consistently decreased in rats, mice and dogs. In conjunction with an increase in reticulocytes, white blood cells were decreased in the dog and increased in the rat. Hematological alterations in rats and mice were considered to be an indication of mild anemia. In mice, the finding of anemia was corroborated by increased spleen weights in conjunction with extramedullary hematopoiesis

in the spleen. In dogs, the presence of reticulocytosis and polychromasia in conjunction with extramedullary hematopoiesis in the spleen was considered indicative of regenerative anemia after subchronic dosing with spinetoram.

The most consistent finding following subchronic and chronic dosing in rats, mice and dogs with spinetoram was vacuolation and/or aggregates of macrophages in a variety of tissues, including endocrine tissues/organs, but primarily those of the lymphoid system. Incidence and severity increased with increasing dose, but did not appear to be affected by the duration of treatment. These findings were also observed in the spinosad toxicology studies which used dose levels, for the most part, similar to those used for spinetoram. In the dog, slight vacuolation of lymphoid macrophages was observed at the low dose, in males only. Similar findings of vacuolation were not observed after chronic dosing with spinetoram; however, this was attributed to dose selection since at a slightly higher dose level in the spinosad chronic dog study, vacuolation of lymphoid tissue was observed. Although a NOAEL for males for the vacuolation findings was not determined in the subchronic study with spinetoram, the combined results of the spinetoram and spinosad dog studies were considered for determination of overall NOAELs for this endpoint.

The vacuolation observed throughout the spinetoram and spinosad databases was purported to be consistent with effects produced by a group of drugs known as the cationic amphiphilic drugs (CAD) and not reflective of a targeted toxicity to the endocrine and lymphoid systems, per se. The molecular structure of a cationic amphiphilic compound consists of a hydrophilic cationic portion containing a primary or substituted nitrogen group and a hydrophobic portion consisting of an aromatic and/or aliphatic ring structure. This group of drugs induces phospholipidosis, a condition resulting from the accumulation of polar lipids within lysosomes due to the CAD-induced impairment of degradation of the sequestered material. The associated abnormal cytoplasmic inclusion bodies that are formed due to the segregation of polar lipids can assume one of two basic morphologic types: multilamellated or crystalloid. Literature references indicate that the extent of cellular alterations are dependent upon the cell type affected. Those cells that are actively phagocytic (i.e. mobile or fixed macrophages in the liver, lung and lymphatic tissues) are known to be affected to a greater extent, although phagocytic activity does not appear to be a prerequisite for extensive cellular lesions. According to the literature, it appears as though the storage of phospholipids is reversible by discontinuing exposure to the compound. Upon lowering the compound concentration in the extracellular space, the diffusion gradient gradually reverses and the usual abilities of the cell will resume, allowing the lipids to be properly utilized and degraded. The rate of reversibility will be determined by the affinity of the compound towards the lipids and the duration of the exposure to the compound. (H. Lullman et al, 1975; Reasor, M.J, 1989; Halliwell, W. H., 1997; H. Lullman et al, 1978; Schneider, P., 1992; Reasor, M.J. and S. Kacew, 2001). The findings in the spinetoram toxicology database suggest that this pesticide behaves in a manner similar to a CAD. Vacuolatory changes examined at the light microscopic level in the 90-day rat study were associated with the accumulation of cytoplasmic lamellar inclusions. Additional assessment of these vacuoles in kidney, lung and spleen with an electron microscope confirmed that lamellar structures were present; however, the exact chemical composition of the cellular contents was not identified. As a result, there remains uncertainty with regards to the proposed mode of action as it relates to effects on several organ systems, including endocrine and lymphoid. For this reason, additional information is required to

identify the nature of the contents of the vacuoles to adequately support the proposed mode of action as being more general in nature without direct consequences to activity of these organ systems. Until such information is provided, the risk assessments will include consideration of this uncertainty.

In addition, the scientific literature indicates that alveolar macrophages may have a pronounced susceptibility to the effects of CADs, likely due to their continuous phagocytic uptake of phospholipid-rich surfactant material from the alveolar lining. (H. Lullman et al, 1975; Reasor, M.J, 1989; Halliwell, W. H., 1997; Reasor, M.J. and S. Kacew, 2001). For this reason, a repeat dose inhalation study is required.

Multifocal degeneration with regeneration of the kidney tubules was also evident in mice after subchronic dosing. In male mice, this effect was observed at the lowest dose level; however, the low incidence and severity (very slight) was similar to what was observed at the mid dose where other signs of toxicity were recorded. This was believed to be a transient adaptive effect, as it was not observed in either the 18-month mouse oncogenicity study with spinetoram or spinosad, both with clearly defined NOAELs.

Several effects were observed in the dog after subchronic dosing with spinetoram including bone marrow necrosis and changes in organ weights. Decreased thymus weights in male dogs were associated with atrophy of the thymic cortex. Liver weights were increased in both male and female dogs after subchronic dosing and in males only (no corresponding histopathology) after chronic dosing with spinetoram. Additionally, chronic dosing in dogs resulted in arteritis accompanied by necrosis of the arterial wall in several tissues.

After treatment with spinetoram, thyroid hormone levels were affected in both studies that measured for this parameter. In the subchronic oral rat study, T_3 was decreased at the two highest dose levels in females only in the absence of other thyroid hormone level changes or histopathological alterations of the thyroid, although colloid depletion in the thyroid was observed in high dose males. In the 2-generation reproduction study, decreased T_4 and/or increased thyroid stimulating hormone (TSH) were observed at the high dose in the first generation parental females and the second generation parental males and females. Thyroid hormone levels were not measured in the pups. For both studies, effects on thyroid hormone levels occurred at the highest doses and in conjunction with other effects. After chronic treatment with spinosad, female rats exhibited increased absolute and relative thyroid weights, but thyroid hormone levels were not measured.

When considered with the spinosad database, the dose levels chosen for the 18-month mouse study with spinetoram were considered adequate. In a rat chronic-carcinogenicity study using spinosad, excessive mortality at the high dose indicated that the maximum tolerated dose had been achieved. Chronic dosing in mice with spinetoram and spinosad provided no evidence of treatment-induced oncogenicity at any dose level tested. Chronic dosing in rats with spinosad also produced no evidence of treatment-induced oncogenicity, which was further supported by the negative findings in genotoxicity studies using spinosad.

No evidence of mutagenic potential of spinetoram was observed in vitro with the Ames bacterial mutation test. Under the conditions of an in vitro mammalian cell gene mutation assay in cultures of Chinese hamster ovary cells, spinetoram was considered non-mutagenic for point mutations, frame-shift mutations and deletions. Spinetoram was non-clastogenic in the presence and absence of metabolic activation in an in vitro chromosomal assay using rat lymphocytes. In an in vivo, mouse micronucleus assay, spinetoram did not induce micronuclei. Based on the data presented, spinetoram was not considered to be genotoxic under the conditions of the tests performed.

There was no evidence of increased susceptibility of the young in developmental toxicity studies in rat and rabbit. As in the subchronic toxicity studies, general toxicity was observed in the dams as decreased body-weight gain and increased liver weight. The rabbit appeared to be more sensitive to spinetoram toxicity than the rat. There were no effects of treatment observed in the fetuses of either rats or rabbits.

In a two-generation reproductive toxicity study, generalized toxicity was observed in parental animals as cytoplasmic vacuolation of thyroid follicular epithelial cells, altered thyroid hormone levels, facial/perineal soiling and increased pigment in the proximal tubule cells/lamina of the kidney. There were no effects observed in the pups, although thyroid hormones were not measured in the offspring. Dams of both generations had an increased incidence of dystocia and abnormal parturition at the lowest observed adverse effects level (LOAEL), causing sacrifice of maternal animals due to moribund condition. Abnormal parturition consisted of prolonged, interrupted and/or incomplete delivery of pups, with some deliveries lasting until lactation day 4. These findings were similar to those observed in the spinosad database, although in addition to moribund sacrifice, there were deaths observed in some dams treated with spinosad at the LOAEL. In addition, increased incidences of post-implantation loss and late absorbing/retained fetuses were observed at the LOAEL with spinetoram.

Following acute and repeated dose neurotoxicity testing, treatment with spinetoram did not result in any neuropathology. A chronic neurotoxicity study was conducted using a group of satellite animals selected from the 2-year chronic/oncogenicity study in rats. Two subsets of animals were examined for either neurobehavioural changes or neuropathology alterations over a one-year period.

Consistent with past PMRA policy and now formalized under the *Pest Control Products Act*, additional factors have also been applied, where warranted, to protect the population from relevant endpoints of concern or any database uncertainty. The standard uncertainty factor (UF) of 100 has been applied to account for interspecies extrapolation and intraspecies variability. For assessing risks from potential residues in food or from products used in or around homes or schools, the *Pest Control Products Act* requires the application of an additional 10-fold factor. This factor should take into account potential prenatal and postnatal toxicity and completeness of the data with respect to the exposure of and toxicity to infants and children. A different factor may be determined to be appropriate on the basis of reliable scientific data.

With respect to the completeness of the toxicity database concerning the exposure of and toxicity to infants and children, extensive data were available for spinetoram. The prenatal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of rat or rabbit fetuses to in utero exposure to spinetoram. There was no indication of increased susceptibility in the offspring compared to parental animals in the reproduction study. On the basis of this information, the 10-fold factor applied under the *Pest Control Products Act* was reduced to 1X.

Results of the acute and chronic tests conducted on laboratory animals with spinetoram and its associated end-use products Radiant SC Insecticide and Delegate WG Insecticide, as well as the toxicological endpoints selected for the human health risk assessment, are summarized in Tables 2, 3 and 4 of Appendix I.

3.2 Determination of Acceptable Daily Intake

The recommended acceptable daily intake (ADI) for spinetoram is 0.008 mg/kg bw/day, based on the calculation shown below. The one-year dog study with spinetoram was considered the most appropriate study to assess chronic dietary exposure. The no observed adverse effects level (NOAEL) was 2.49 mg/kg bw/day, based on arteritis accompanied by necrosis of the arterial wall in various tissues at 5.36 mg/kg bw/day. The standard UF of 100 has been applied to account for intraspecies variability and interspecies extrapolation in toxicological responses when exposed to a chemical substance. An additional database factor of 3 was applied to account for the residual uncertainty regarding the mode of action of spinetoram (identification of content of vacuoles) resulting in a total UF of 300.

The ADI is calculated according to the following formula:

$$\text{ADI} = \frac{\text{NOAEL}}{\text{UF}} = \frac{2.49 \text{ mg/kg bw/day}}{300} = 0.008 \text{ mg/kg bw/day of spinetoram}$$

This ADI provides margins of safety (MOS) ≥1200 to the NOAEL for dystocia and thyroid effects in the reproduction study and a MOS ≥ 600 for the NOAEL for bone marrow necrosis in the subchronic dog study.

3.3 Determination of Acute Reference Dose

Due to the low acute toxicity of spinetoram following acute oral, dermal and inhalation exposure, an acute reference dose is not required.

3.4 Occupational and Residential Risk Assessment

3.4.1 Toxicological Endpoints

Occupational exposure to spinetoram is characterized as short- to intermediate-term in duration and is predominately by the dermal and inhalation routes. Where appropriate, consideration was given to the results of the spinosad toxicology database in endpoint selection.

Short-term to Intermediate-term Dermal Endpoint:

A NOAEL of 1000 mg/kg bw/day from the 28-day dermal toxicity study with spinetoram was used for both dermal exposure scenario durations for the following reasons:

The study was well-conducted and included histopathology examinations of the target tissues of toxicity, including kidney and thyroid. While relevant for the short-term exposure scenario, this study was also considered appropriate for the intermediate term scenario as there did not appear to be any significant durational effects observed in the database. However, this study was not designed to assess reproductive parameters and it did not include measurements of thyroid hormone levels, endpoints identified at a dose of 75 mg/kg bw/day in the 2-generation reproduction study with spinetoram. The NOAEL for this effect was 10 mg/kg bw/day. To ensure that the altered hormone levels and dystocia observed in the 2-generation reproduction study were adequately considered, additional effects observed at the same or lower dose levels in the reproduction study were used as biomarkers for these endpoints of concern. For this purpose, facial/perineal soiling and increased pigmentation in the kidneys were used as an indication of toxicity at the same dose level where incidences of dystocia occurred. In addition, the results of the 90-day rat study revealed that histopathological alterations in thyroid (vacuolation) were occurring at doses (32/40 mg/kg bw/day) well below those at which any changes in thyroid hormones were reported (128/159 mg/kg bw/day). None of these effects (clinical signs, kidney and thyroid pathology) were observed in the 28-day dermal study, providing assurance that selection of the NOAEL from the dermal study affords protection to the reproductive and thyroid hormone endpoints.

A comparison of NOAEL/LOAEL for the oral and dermal 28-day studies in rats suggests low apparent dermal absorption (in the range of 1–5%). In addition, the lack of systemic toxicity in the 28-day dermal study at the limit dose of 1000 mg/kg bw/day suggests low dermal absorption. Although dermal toxicokinetic data were not available, the results of the oral toxicokinetic studies did not suggest significant bioaccumulation following repeated oral dosing.

In light of the above, a target margin of exposure (MOE) of 100 is recommended based on a 100-fold uncertainty factor to account for expected differences in toxicological response within and between species.

Short-term to Intermediate-term Inhalation Endpoint:

No repeat dose inhalation studies were available for consideration and therefore it was considered appropriate to default to an oral study for endpoint selection. The dog was the most sensitive species to the toxic effects of spinosad and spinetoram with an overall NOAEL of 4.9 mg/kg bw/day from the 90-day oral dog study with spinosad. This study and NOAEL was selected for the short-term to intermediate-term inhalation endpoint. The duration of exposure was applicable and in addition to general signs of toxicity, the predominant database effect of vacuolation in several tissues was observed at the LOAEL of 9.7 mg/kg bw/day.

A target MOE of 300 is recommended based on a 100-fold uncertainty factor to account for expected differences in toxicological response within and between species with an additional database factor of 3 to account for the residual uncertainty regarding the mode of action of spinetoram (impact on determination of targeted effects on immune and endocrine systems). A repeat dose inhalation study is required in light of information in the scientific literature which suggests that alveolar macrophages may be more susceptible to the toxic effects of CAD-like substances.

3.4.2 Occupational Exposure and Risk

3.4.2.1 Handler Exposure and Risk

A crop grouping approach was used to derive handler exposure estimates using the highest area treated per day for each crop group. Airblast application was assumed for pome fruit, stone fruit and grapes; for all other crops, groundboom application was assumed. Default area treated per day values were used to estimate dermal and inhalation exposure. The clothing scenario used is coveralls over a single layer of clothing and gloves for mixing and loading. For groundboom and airblast application, the clothing scenario used is a single layer without gloves.

Dermal and inhalation MOEs for all mixer/loader and applicator scenarios proposed for Radiant SC Insecticide and Delegate WG Insecticide are above the target MOEs (dermal MOEs are >37 000; inhalation MOEs are >4500).

3.4.2.2 Postapplication Exposure and Risk

A tier one risk assessment was performed for workers entering field crops treated with three applications of Radiant SC Insecticide or Delegate WG Insecticide made 3-7 days apart. A crop grouping approach was used to derive exposure estimates using the most conservative transfer coefficient for each crop group.

Postapplication risk estimates for workers entering areas treated with Radiant SC Insecticide and Delegate WG Insecticide are above the target MOE of 100 (MOEs are >4700).

3.4.3 Residential Exposure and Risk

3.4.3.1 Handler Exposure and Risk

There are no domestic class products; therefore, a residential handler assessment was not required.

3.4.3.2 Postapplication Exposure and Risk

There is potential to adults and children entering pick-your-own facilities to hand harvest apples, strawberries and raspberries. Since there are no acute dermal or oral toxicological concerns for spinetoram, a risk assessment for pick-your-own scenarios is not required.

3.4.4 Bystander Exposure and Risk Assessment

For bystanders, exposure is expected to be negligible, based on label directions intended to minimize spray drift.

3.5 Food Residues Exposure Assessment

3.5.1 Residues in Plant and Animal Foodstuffs

The residue definition for risk assessment and enforcement in plant products is parent spinetoram (XDE-175-J, XDE-175-L) and two metabolites N-demethyl-175-J (ND-J) and N-formyl-175-J (NF-J). The residue definition for enforcement in animal commodities and for risk assessment in ruminant commodities is XDE-175-J, XDE-175-L, ND-J and NF-J. The residue definition for risk assessment in poultry commodities is XDE-175-J, XDE-175-L, ND-J, NF-J, 3'-O-deethyl-175-J, 3'-O-deethyl-175-L and O-demethyl-175-L. The data gathering/enforcement analytical methodology, LC-MS/MS, is valid for the quantification of spinetoram residues in wet crop, dry crop, acidic crop, oily crop and livestock matrices: bovine (muscle, kidney, liver), poultry (muscle, liver), milk and egg. The residues of spinetoram are stable in plant matrices when stored in a freezer at –20°C for 12 months. Spinosad residue data and MRLs were translated to spinetoram for two reasons: spinetoram and spinosad are structurally similar tetracyclic macrolide fermentation products of *Saccharopolyspora spinosa* and side-by-side supervised residue trials conducted using spinetoram and spinosad on apple, leaf lettuce, sugar beet, tomato and orange throughout the United States and Canada are adequate to support the translation of data. Bulb vegetables, mint and herbs could not be supported due to a lack of residue data.

3.5.2 Dietary Risk Assessment

A chronic dietary risk assessment was conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.0), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.5.2.1 Chronic Dietary Exposure Results and Characterization

The following assumptions were made in a refined chronic analysis: median residues of spinetoram, % crop treated, anticipated residue values for all animal commodities. The refined chronic dietary exposure from all supported spinetoram food uses (alone) for the total population, including infants and children and all representative population subgroups are 66% of the acceptable daily intake (ADI). Aggregate exposure from food and water is considered acceptable. The PMRA estimates that chronic dietary exposure to spinetoram from food and water is 22% (0.001753 mg/kg bw/day) of the ADI for the total population. The highest exposure and risk estimate is for children 1–2 yrs old at 67% (0.005322 mg/kg bw/day) of the ADI.

3.5.2.2 Acute Dietary Exposure Results and Characterization

No appropriate endpoint attributable to a single dose for the general population (including children and infants) was identified. Therefore, no acute dietary exposure assessment was conducted.

3.5.3 Aggregate Exposure and Risk

The aggregate risk for spinetoram consists of exposure from food and drinking water sources only. There are no residential uses. Aggregate risks were calculated based on chronic endpoint. An acute endpoint was not identified for the general population, including infants and children.

3.5.4 Maximum Residue Limits

Table 3.5.4.1 Proposed Maximum Residue Limits

MRLs (ppm)	Foods
7	Leafy Brassica greens (crop subgroup 5B: bok choy, Chinese cabbage, broccoli raab, collards, kale, mustard greens, mustard spinach, rape greens); Leafy vegetables (crop group 4: amaranth, arugula, cardoon, celery, celtuce, Chinese celery, corn salad, dandelion leaves, dock, edible leaved chrysanthemum, endives, fresh chervil leaves, fresh Florence fennel leaves and stalk, garden cress, garden purslane, garland chrysanthemum, head lettuce, leaf lettuce, New Zealand spinach, orach leaves, parsley leaves, radicchio, rhubarb, spinach, Swiss chard, upland cress, vine spinach, winter purslane); leaves of root and tuber vegetables (crop group 2: black salsify tops, cassava leaves, celeriac tops, chicory tops, edible burdock tops, garden beet tops, oriental radish tops, radish tops, rutabaga tops, tanier leaves, taro leaves, turnip tops, turnip-rooted chervil tops).
3	Citrus oil

MRLs (ppm)	Foods
2	Head and stem Brassica vegetables (crop subgroup 5A: broccoli, Brussels sprouts, cabbages, cauliflower, Chinese broccoli, Chinese mustard cabbage, kohlrabi, Napa Chinese cabbage).
1	Grape juice
0.7	Raisins; low growing berry subgroup [crop subgroup 13-07G (except blueberry, lowbush; cranberry): bearberry; bilberry; cloudberry; lingonberry; muntries; partridgeberry; strawberry; cultivars, varieties, and/or hybrids of these.]
0.5	Caneberry subgroup (crop subgroup 13-07A: blackberry; loganberry; raspberry, red and black; wild raspberry; cultivars, varieties, and/or hybrids of these.), bushberry subgroup [crop subgroup 13-07B (except cranberry, highbush; lingonberry): Aronia berry; blueberry, highbush; blueberry, lowbush; buffalo currant; Chilean guava; currant, black; currant, red; elderberry; European, barberry; gooseberry; honeysuckle, edible; huckleberry; jostaberry; Juneberry; native currant; salal; sea buckthorn; cultivars, varieties, and/or hybrids of these.]
0.4	Small fruit vine climbing subgroup except fuzzy kiwifruit [crop subgroup 13-07F (except gooseberry): Amur river grape; grape; kiwifruit, hardy; Maypop; schisandra berry; cultivars, varieties, and/or hybrids of these.]
0.3	Cucurbit vegetables [crop group 9: balsam apples, balsam pears, cantaloupes, chayote fruit, Chinese cucumbers, Chinese waxgourds, citron melons, cucumbers, edible gourds (other than those listed in this item), muskmelons (other than those listed in this item), pumpkins, summer squash, watermelons, West Indian gherkins, winter squash]; edible-podded legume vegetables (crop subgroup 6A: edible-podded dwarf peas, edible-podded jackbeans, edible-podded moth beans, edible-podded peas, edible-podded pigeon peas, edible-podded runner beans, edible-podded snap beans, edible-podded snow peas, edible-podded soybeans, edible-podded sugar snap peas, edible-podded swordbeans, edible-podded wax beans, edible-podded yardlong beans); citrus (crop group 10: calamondins, citrus citron, citrus hybrids, grapefruits, kumquats, lemons, limes, oranges, pummelos, satsuma mandarins, tangerines)
0.2	Fruiting vegetables (crop group 8: bell peppers, eggplants, groundcherries, non-bell peppers, pepinos, pepper hybrids, tomatillos, tomatoes); okra; stone fruits (crop group 12: apricots, nectarines, peaches, plumcots, plums, prune plums, sweet cherries, tart cherries).

MRLs (ppm)	Foods
0.1	Pome fruits (crop group 11: apples, crabapples, loquats, mayhaws, oriental pears, pears, quinces); root vegetables (crop subgroups 1A&1B: black salsify roots, carrot roots, celeriac roots, chicory roots, edible burdock roots, garden beet roots, ginseng roots, horseradish roots, oriental radish roots, parsnip roots, radish roots, rutabaga roots, salsify roots, skirret roots, Spanish salsify roots, sugar beet roots, turnip roots, turnip-rooted chervil roots, turnip-rooted parsley roots); wheat, barley, oat, rye.
0.04	Asparagus; corn (field, sweet, pop); cranberry; tuberous and corm vegetables (crop subgroups 1C&1D: arracacha, arrowroot, cassava roots, chayote roots, Chinese artichokes, chufa, edible canna, ginger roots, Jerusalem artichokes, lerens, potatoes, sweet potato roots, tanier corms, taro corms, true yam tubers, turmeric roots, yam bean roots); succulent shelled pea and bean (crop subgroup 6B: succulent shelled blackeyed peas, succulent shelled broad beans, succulent shelled English peas, succulent shelled garden peas, succulent shelled green peas, succulent shelled lima beans, succulent shelled peas, succulent shelled pigeon peas, succulent shelled southern peas); dried shelled pea and bean, except soybean (crop subgroup 6C: dry adzuki beans, dry beans, dry blackeyed peas, dry broad beans, dry catjang seed, dry chickpeas, dry field peas, dry guar seed, dry kidney beans, dry lablab beans, dry lentils, dry lima beans, dry moth beans, dry mung beans, dry navy beans, dry pigeon peas, dry pink beans, dry pinto beans, dry rice beans, dry southern peas, dry tepary beans, dry urd beans, grain lupin, mung bean sprouts); soybean.
7.5	Milk, fat
5.5	Fat of cattle, goats, sheep and horses.
0.85	Liver of cattle, goats, sheep and horses.
0.6	Meat byproducts of cattle, goats, sheep and horses.
0.3	Milk
0.2	Meat of cattle, goats, sheep and horses.
0.04	Meat, meat byproducts and fat of hog and poultry, egg

Crop Groups are listed in Appendix III.

For additional information on Maximum Residue Limits (MRL) in terms of the international situation and trade implications, refer to Appendix II.

The nature of the residues in animal and plant matrices, analytical methodology, field trial data and the chronic dietary risk estimates are summarized in Tables 1, 5 and 6 in Appendix I.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

4.1.1 Abiotic Transformation

Spinetoram (XDE 175-J and -L) was stable to hydrolysis in acid and neutral conditions (Appendix I, Table 7). Under alkaline conditions, it hydrolyzed slowly with a first order linear half-life of 158 days and, is therefore, considered stable. One major transformation product, N-demethyl-175-L (maximum of 11.9% of the applied active at 30 days) and one minor transformation product, N-demethyl-175-J (6.7% of the applied active at 30 days) were detected under alkaline conditions (Appendix I, Table 7). These results indicate that hydrolysis would not be a principle route of transformation in the environment.

Spinetoram phototransformed in soils with first order linear half-lives of 20.8 (L) and 69.4 (J) days, based on a 12-hour light/12-hour dark cycle (Appendix I, Table 7). No transformation products were detected either in the irradiated or in dark control soils. At study termination, total $^{14}CO_2$ evolved ranged from 1.9–3.5% of the applied active from the irradiated soil and <0.1% from the corresponding dark controls. In the irradiated samples, concentration of spinetoram decreased from 93.2–97.1% of the applied at 0 days to 25.7–25.9% at 18 days.

In aquatic systems, spinetoram phototransformed rapidly with first order linear half-lives of <1 day, based on a 12-hour light/12-hour dark cycle (Appendix I, Table 8). No residues of parent compound were detected in the samples after two days of irradiation. Two major transformation products were detected (Appendix I, Table 8); N-demethyl-175-L with a maximum of 12.2% and no residues after 4 days and one unidentified compound with a maximum of 10.8% of the applied active and <1% at 19 days (study termination). Minor transformation products detected were N-demethyl-175-J (6.6% of applied active) and unidentified products. XDE-175-L was stable in the dark controls. Phototransformation in the aquatic systems would be a principle route of transformation in the environment.

4.1.2 Biotransformation

Spinetoram biotransformed rapidly in soils under aerobic conditions with half-lives of 9–31 days for XDE-175-J and 3-15 days for XDE-175-L, respectively (Appendix I, Table 7). XDE-175-L degraded slightly faster than XDE-175-J. At the end of the 366 day study period, less than 3% of the residues of parent compound were observed. These values indicate that spinetoram is

non-persistent to slightly persistent in soils under aerobic conditions. Two major transformation products, N-demethyl-175-J (maximum of 69.7% of the applied active and 42% at 366 days) and N-demethyl-175-L (maximum of 43.8% of applied active and 9.7% at 366 days) were detected in soils (Appendix I, Table 7). No minor products were identified. The evolved $^{14}CO_2$ ranged from 7.7 to 37% of the applied active.

In sediment/water systems under aerobic conditions, spinetoram biotransformed with DT_{50} values of 116–119 days for XDE-175-J and 124–131 days for XDE-175-L. These values indicate that spinetoram is moderately persistent in aquatic systems under aerobic conditions. The half-life values are well beyond the study period of 30 days and therefore, for modelling purposes spinetoram is considered as stable. Following application, spinetoram partitioned significantly into sediment (<6.7% and < 2.7% of the applied active was observed in the water layer at 0-day and after 30 days of its application). Two major transformation products, N-demethyl-175-J (9.7%) with the XDE-175-J study and N-demethyl-175-L (12.9%) with XDE-175-L study and one minor product, O-demethyl-175-J (or isomer of) were detected (Appendix I, Table 8). All three compounds were detected only in the sediment.

Under anaerobic conditions, XDE-175-J transformed slowly in the whole sediment/water system with DT_{50} values of 385-416 days for XDE-175-J and 1348–1386 days for XDE-175-L (Appendix I, Table 8). At the end of the 365 day study period, concentration of parent compounds ranged from 48.9 to 76.7% of the applied dose. These values indicate that spinetoram is persistent in aquatic systems under anaerobic conditions. Following application, spinetoram (XDE-175 -J and -L) rapidly partitioned from water layer into sediment. Two major transformation products, O-demethyl-175-J (27.3%) with the XDE-175-J study and O-demethyl-175-L (10.5%) with XDE-175-L were detected in the sediments (Appendix I, Table 8). No minor transformation products were detected.

4.1.3 Mobility

The Freundlich adsorption K_d values for the parent compound for loamy sand, silt loam, sandy loam, and loam soils were 11–19, 272–300, 17–25 and 10–22 respectively; the corresponding adsorption K_{oc} values were 1375–2375, 24727–27273, 2429–3571 and 2000–4400 (Appendix I, Table 7). These values indicate that spinetoram is immobile in silt loam soils and has slight to low mobility in other soils. According to these adsorption values, spinetoram is considered to have a low potential to leach and contaminate the ground water. At the end of adsorption phase, 46.7–94.8% of the applied active was adsorbed. During the desorption phase, 2.9 to 20.4% of the adsorbed was desorbed.

The adsorption K_d values for the transformation product, N-demethyl-175-J were 16, 133, 32 and 8 for the loamy sand, silt loam, sandy loam and loam soils, respectively; the corresponding adsorption K_{oc} values were 2062, 12127, 4642 and 1631. These values indicate that N-demethyl-175-J is immobile in silt loam soils and has slight to low mobility in other soils. N-demethyl-175-J has, therefore, a low potential to leach and contaminate groundwater. At the end of the adsorption phase, 42.6–88.6% of the applied N-demethyl-175-J was adsorbed.

The adsorption K_d values for the transformation product, N-demethyl-175-L were 34, 340, 81 and 19 for the loamy sand, silt loam, sandy loam and loam soils, respectively; the corresponding adsorption K_{oc} values were 4270, 30918, 11559 and 3718. These values indicate that N-demethyl-175-L is immobile in silt loam and sandy loam soils and has slight to low mobility in other soils. N-demethyl-175-J has, therefore, a low potential to leach and contaminate groundwater. At the end of the adsorption phase, 61.1–90.2% of the applied N-demethyl-175-L was adsorbed.

Spinetoram is essentially non-volatile and no significant volatilization is expected. Atmospheric contamination is not considered to be a route of exposure with the proposed use.

4.1.4 Dissipation and Accumulation Under Field Conditions

Terrestrial: Under Canadian field conditions, spinetoram dissipated rapidly from soils with DT_{50} values of less than one day (Appendix I, Table 7). No residues of parent compound were detected in soils after 3-14 days of its application. These values indicate that spinetoram is non-persistent in soils under field conditions. One major transformation product, N-demethyl-J, was detected at a maximum concentration of 12.5% of the applied parent compound (Appendix I, Table 7). It dissipated (biphasic) in soils with half-lives of 8.5–12.3 days. At the Ontario site, no residues were detected after 14 days of its application, whereas at the PEI site, its concentration reduced to 6.2% of the applied active at the end of the study duration of 462 days. Neither the parent compound nor the transformation product were detected in soil beyond 15 cm soil depth, which indicate that these compounds have a low potential to leach and contaminate the ground water.

The DT_{75} values of 2–5 days and no residues at 7–14 days after application indicate that spinetoram has a low potential for residue carryover. For the transformation product, N-demethyl-J, the DT_{75} values of up to 400 days indicate a potential for residue carryover. The actual concentration was, however, only 0 to 6.2% of the applied at the end of 462-day study period and therefore, the potential for carryover is limited. The major route of dissipation of spinetoram under terrestrial field conditions appears to be transformation.

The behaviour of spinetoram with respect to persistence, residue carryover, leaching and formation of transformation products, under U.S. field conditions is similar to that of Canadian field conditions.

Aquatic: Under U.S. aquatic field conditions, spinetoram dissipated very rapidly with half-lives of 18.1–20.4 hours. Spinetoram is, therefore, non-persistent in aquatic field conditions (Appendix I, Table 9). Residues of parent compound declined to approximately 12–15% by the end of the study period at 24 hours post-treatment and no partitioning of residues into the sediment was observed. Spinetoram has, therefore, a low potential for residue carryover. One major transformation product, N-demethyl-175-J (maximum of 37.3% and decreased to 13–27% at 24 hours) and one minor product, N-methyl-175-L (maximum of 5.7% and decreased to 3.67–2.24% at 24 hours) were detected (Appendix I, Table 9). Total N-demethyl 175-J and N-demethyl-175-L residues dissipated with a half-life value of 31.1 hours following the

maximum detection at 30 minutes post-treatment. Transformation products are, therefore, considered non-persistent in aquatic systems under field conditions.

4.1.5 Bioaccumulation

In fish exposed to [^{14}C]XDE-175-J and [^{14}C]XDE-175-L at a low dose (17.3–22.3 ng/mL), the maximum total [^{14}C]residues were 185–711 ng/g in the edible tissue, 953–2090 ng/g in nonedible tissue and 826–2086 ng/g in whole fish. The corresponding bioconcentration factors (BCFs) were 11–104, 53–330 and 46–344, respectively. After 21 days of depuration in the low-dose study, total [^{14}C]residues had decreased by approximately 88%. The elimination half-lives for [^{14}C]residues in edible tissue, nonedible tissue and whole fish were 2.3–4.5, 4.1–3.9 and 4.1 days, respectively.

In the fish exposed at a high dose (96.6–102 ng/mL), the maximum total [^{14}C]residues were 4577–17957 ng/g in the edible tissue, 10942–26831 ng/g in the nonedible tissue and 9136–24443 ng/g in whole fish. The corresponding BCFs were 43–214, 103–430 and 86–348, respectively (Appendix I, Table 8). After depuration, total [^{14}C]residues had decreased by 33.2–87.9%. The elimination half-life for [^{14}C]residues in whole fish, edible tissue and nonedible tissue were 5.0–5.2, 4.5 and 5.3 days, respectively.

The BCF values indicate that spinetoram has a low potential for bioaccumulation in organisms.

4.1.6 Summary of Fate and Behaviour in the Environment

Terrestrial environment: Spinetoram rapidly transforms in soils and is non-persistent in the terrestrial environment (lab t ½: 3–31 days and field DT_{50}: < 1 day). Hydrolysis and phototransformation would not be principle routes of transformation in the terrestrial environment. It is stable to hydrolysis under acid and neutral conditions but slowly hydrolyzes under alkaline conditions (pH 9: t½ 158 days) with the formation of one major transformation product, N-demethyl-175-L and one minor product, N-demethyl-175-J. Biotransformation would be a principle route of transformation in soils under aerobic conditions. It transforms rapidly (t½: 3–31 days) and forms two major transformation products, N-demethyl-175-J and N-demethyl-175-L. Spinetoram (adsorption K_d: 10–300 and K_{oc}: 1375–27273) and the transformation products, N-demethyl-175-J (adsorption K_D: 8–133) and N-demethyl-175-L (adsorption K_d: 19–340) are immobile to low mobility in soils.

Under Canadian field conditions, spinetoram is non-persistent (DT_{50}: < 1 day) and has a low potential for residue carryover (DT_{75}: 2–5 days and no residues detected after 7–14 days of its application). It forms one major transformation product, N-demethyl-J which is non-persistent (field DT_{50}: 8.5–12.3 days) under field conditions. Although the DT_{75} value of 400 days indicate that it has a potential for residue carryover, its actual concentrations in soils (0–6% at the end of 462 days) indicate a limited potential for carryover. No residues of spinetoram and its transformation products were detected beyond 30 cm soil depth under field conditions, which indicate that they have a low potential to leach and contaminate groundwater. These results are in agreement with those of laboratory soil adsorption studies. The major route of dissipation of

spinetoram under terrestrial field conditions would be transformation. Field studies also indicated that the behaviour of spinetoram under U.S. field conditions is similar to that of Canadian field conditions.

Aquatic environment: With the proposed use pattern, spinetoram can enter into aquatic systems by drift or surface runoff. Hydrolysis would not be a principle route of transformation in the aquatic environment. It is stable to hydrolysis under acid and neutral conditions but slowly hydrolyzes under alkaline conditions (pH 9: t½ 158 days) with the formation of one major transformation product, N-demethyl-175-L and one minor product, N-demethyl-175-J. Phototransformation would be a principle route of transformation in the aquatic environment (t½: < 1 day) and forms one major transformation product, N-demethyl-175-L and one minor transformation product, N-demethyl-175-J. Laboratory biotransformation studies indicated that spinetoram is moderately persistent and persistent in aquatic systems under aerobic and anaerobic conditions, respectively. It forms two major transformation products, N-demethyl-175-J and N-demethyl-175-L under aerobic conditions and O-demethyl-175-J and O-demethyl-175-L under anaerobic conditions.

In aquatic field conditions, spinetoram dissipates very rapidly (DT_{50}: 18.1–20.4 hours) and is non-persistent. It does not partition to the sediments. Spinetoram has a low potential for residue carryover (residues:12–15% at the end of 24 hours). It forms one major transformation product, N-demethyl-J and one minor product, N-demethyl-175-L and both are non- persistent (combined DT_{50}: 31.1 hours).

Although the *n*-octanol/water partition coefficient values (log K_{ow} : 4.09 to 4.82 in neutral-alkaline conditions) indicate a potential for bioaccumulation, actual studies on bioaccumulation in fish (high dose BCF 43–430; elimination half-lives: 2.3–5.3 days and field DT_{50}: 20 hours) indicated a low potential for bioaccumulation in organisms.

Air: Spinetoram has a low vapour pressure ($4.2–6.0 \times 10^{-5}$ Pa at 25 °C) and a low Henry's law constant ($3.913–4.938 \times 10^{-8}$ atm.m^3/mole). These values indicate that spinetoram is essentially non-volatile and no significant volatilization is expected. Atmospheric contamination is, therefore, not considered to be an important route of exposure with the proposed use.

4.1.7 Expected Environmental Concentrations

Soil: With the maximum application rate of 105 g a.i./ha applied three times with seven day intervals, the EEC in soil would be 0.12 mg a.i./kg soil.

Aquatic systems: Assuming a direct over spray with maximum application rates on a water body of 15 cm and 80 cm depth, the EECs would be 0.07 and 0.013 mg a.i./L, respectively.

Ecoscenario: An aquatic ecoscenario assessment using the Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS) was conducted to estimate the EECs in a shallow receiving water body due to runoff from the treated area. The highest 90th percentiles of the peak and the time-averaged concentrations were estimated in 80 cm deep (represents a permanent wetland) and 15 cm deep (seasonal water body to assess the risk to amphibians) (Appendix I, Table 10).

Vegetation and other food sources: Concentrations of spinetoram residues on plants and other food sources (Appendix I, Tables 11 and 12) were estimated assuming a direct overspray of maximum application rates per year on food sources.

4.2 Effects on Non-Target Species

A quotient method is used to estimate risk of potential adverse effects on non-target species. The risk quotient (RQ) is calculated by dividing the exposure estimate by a value representing a toxicity endpoint. A screening-level risk assessment is initially performed using the EECs for a very conservative scenario (e.g. direct overspray of a body of water) and the most sensitive toxicity endpoint. Low risk is predicted if the risk quotient is less than the trigger value of one. In these cases, no further assessment is done. For those groups of organisms for which the RQ is greater than one, a refined assessment is undertaken. A refined assessment takes into consideration more realistic exposure scenarios (e.g. drift to non-target habitats and runoff to water bodies) and may consider different toxicity endpoints.

4.2.1 Effects on Terrestrial Organisms

Data on toxicity to earthworm (acute and chronic), bees (acute oral and contact and foliar residues), wild birds (acute, dietary and reproductive) and mammals and terrestrial plants were submitted. See Appendix I, Tables 13 and 15 for details.

Soil organisms: Spinetoram has no acute and chronic adverse effects on earthworms up to 1000 and 18.65 mg a.i./kg soil, respectively. The acute RQ (0.0001) and chronic RQ (0.006) values indicate that spinetoram will pose a negligible risk to earthworms with the proposed use.

Bees: The acute oral and contact LD_{50} for bees were 0.11 and 0.024 µg a.i./bee, respectively. At 110 g a.i./ha, no adverse effects on bees due to foliar residues were observed. The most sensitive parameter with bees is the acute contact with a NOEL of 0.0065 µg a.i./bee (0.0073 kg a.i./ha) and the proposed application rate is 0.272 kg a.i./ha. The RQ value of 37.26 indicates that the proposed use of spinetoram formulation as an insecticide would pose a risk to honey bees.

Predatory and parasitic arthropods: Risk to predatory and parasitic arthropods could not be assessed as no toxicity data were submitted. Spinetoram is an insecticide and it is, therefore, expected to have toxic effects on these organisms.

Wild birds: Risk to birds was assessed using the NOEL/NOEC for two bird species, bobwhite quail and mallard duck. The proposed use of spinetoram suggests that exposure is likely to occur through the consumption of treated foliage and associated avian food sources, with the greatest risk arising from oral ingestion of treated foliage. Dietary intake (DI) was estimated from the information on the food consumption (FC) and the EEC of spinetoram in the diet of birds (DI = FC × EEC).

The acute LD_{50} of XDE-175 to bobwhite quail and mallard duck was greater than 2250 mg a.i./kg bw. The acute NOEL for bobwhite quail (most sensitive species) and mallard duck were 292 and 2250 mg a.i./kg bw, respectively. The DI (daily intake) at the proposed maximum application rate is 0.723 mg a.i./ind/d. As the number of days of intake of spinetoram required to reach NOEL is 68.2 days (NOEL(ind)/DI), the birds are not at potential risk on an acute basis. The mallard duck also is not at risk with the proposed use (588 days required to reach NOEL).

On a short-term dietary basis, the LC_{50} for bobwhite quail and mallard duck (most sensitive species) were greater than 5790 and 5640 mg a.i./kg diet, respectively. The corresponding NOEC values were 1810 and 1770 mg a.i./kg diet, respectively. The EEC of spinetoram in the diet with the proposed maximum application rate is 9.18 mg a.i./kg diet. The RQ of 0.005 for the mallard duck and 0.03 for the bobwhite quail indicates that the concentration in the diet is much lower than the NOEC and that ingestion of this compound through the diet with the proposed maximum application rate will pose a negligible risk to wild birds.

No adverse effects on reproductive performance were observed in bobwhite quail and mallard duck up to 1000 mg a.i./kg diet. The RQ of 0.01 for the bobwhite quail and mallard duck indicates that ingestion of this compound with the proposed maximum application rate will pose a negligible risk to reproductive performance of wild birds.

Wild mammals: Risk to mammals was assessed using NOEL/NOEC values obtained from studies with the rat and mouse. The most likely major route of exposure of wild mammals to spinetoram is through dietary sources, i.e., ingestion of treated foliage.

The acute LD_{50} with rat was 5000 mg a.i./kg bw. As no acute NOEL for rat was reported, 1/10th of LD_{50} value, i.e., 500 mg a.i./kg bw, was taken for the RQ calculations. The EEC in a typical rat diet is 9.18 mg a.i./kg diet and the DI is 0.551 mg a.i./ind/d. The maximum number of days of intake of spinetoram that will result in observable effects on rats is 318 days and the wild mammals are, therefore, not at risk on an acute basis.

On a short-term basis, the dietary NOEC with rat and mouse were 120 and 50 mg a.i./kg diet, respectively. The corresponding RQ values of 1.14 and 2.72 indicate that ingestion of this compound at the indicated levels will pose a risk to wild mammals on a short term dietary basis.

The reproductive NOEC for rat was 170 mg a.i./L. The RQ of 0.81 indicates that ingestion of spinetoram at the proposed maximum application rates will pose a negligible risk to reproductive performance of wild mammals.

Non-target terrestrial plants: The adverse effects of the spinetoram-formulation, GF-1640 (25% a.i), on the plant growth parameters were tested in ten crop species at a single rate of 0.150 kg a.i./ha. The EC_{25} value for seedling emergence and vegetative vigour was 0.150 kg a.i./ha. The proposed cumulative application rate is 0.272 kg a.i./ha. The RQ value of 1.81 indicates that the proposed use of spinetoram would adversely affect the terrestrial plants.

4.2.2 Effects on Aquatic Organisms

Data on acute and chronic toxicity to freshwater invertebrates, benthic organisms, freshwater fish, marine invertebrates, marine fish and effects on freshwater plants, freshwater and marine algae were submitted. No acceptable data were submitted on acute toxicity to fresh water invertebrates and cold water fish. See Appendix I, Tables 14 and 16 for details.

Freshwater invertebrates: A study was submitted on acute toxicity of spinetoram to *Daphnia* under static conditions and the study was not acceptable due to an insufficient number of treatment levels. The study must be repeated with the appropriate number of treatment levels. Spinetoram would adversely affect freshwater invertebrates on a chronic basis at concentrations greater than 0.000062 mg a.i./L (NOEC). Screening level risk assessment (RQ: 217) indicated that the proposed use of spinetoram will pose a risk to freshwater aquatic invertebrates on a chronic basis with the proposed maximum application rate.

Spinetoram is non-persistent in aquatic systems under field conditions. Acute toxicity end points are, therefore, more appropriate to estimate the exposure and risk. However, as no acceptable acute study was submitted, chronic exposure data was used to assess the risk on an interim basis.

Benthic organisms: Spinetoram would adversely affect the freshwater benthic organisms (*Chironomus* midge) at concentrations greater than 0.0957 and 0.0016 mg a.i./L in sediments and pore water, respectively (NOECs). Screening level risk assessment (RQ: 8.13) indicated that the proposed use of spinetoram will pose a risk to benthic organisms on a chronic basis.

Amphibians: No data were submitted on toxicity of spinetoram to amphibians. The most sensitive fish toxicity endpoint, i.e., acute LC_{50} of 2.68 µg a.i./L for bluegill sunfish, was used as a surrogate for amphibians. The exposure to amphibians was estimated by calculating the EECs in 15 cm water depth. The RQ value of 0.26 indicated that spinetoram will pose a negligible risk to amphibians on an acute basis. Chronic RQ value of 1.72, however, indicates that the proposed use will pose a risk to amphibians on a chronic basis.

Freshwater fish: A study was submitted on acute toxicity of spinetoram to cold water fish, rainbow trout, under static conditions and the study was not acceptable due to an insufficient number of treatment levels. The study must be repeated with the appropriate number of treatment levels. Toxicity end points of warm water fish were used as the most sensitive end points for fish acute risk assessment.

The NOEC and LC_{50} values for warm water fish, bluegill sunfish, were <0.988 and 2.69 mg a.i./L, respectively. Spinetoram would adversely affect fish (fathead minnow) on a chronic basis at concentrations greater than 0.186 mg a.i./L. Screening level risk assessment (acute RQ: 0.05 and chronic RQ: 0.07) indicated that spinetoram will pose a negligible risk to warm water fish on acute and chronic basis at the proposed maximum application rate.

Freshwater algae: The most sensitive freshwater algal species to spinetoram was green algae with NOEC and EC_{50} values of 0.152 and 0.620 mg a.i./L, respectively. With freshwater diatom, the NOEC and EC_{50} were 0.013 mg and 0.13 mg a.i./L, respectively. Screening level risk assessment (diatom RQ: 0.10) indicates that the proposed use of spinetoram will pose a negligible risk to freshwater diatom and algae.

Freshwater vascular plants: The NOEC and EC_{50} values for vascular plant *Lemna gibba*, were 6.63 and >14.2 mg a.i./L, respectively. Screening level risk assessment (RQ: 0.002) indicated that the proposed use of spinetoram will pose a negligible risk to aquatic plants.

Marine fish: The acute NOEC and LC_{50} values for the marine fish (sheepshead minnow) were 1.8 and 7.87 mg a.i./L, respectively and no adverse affects were observed up to 1.73 mg a.i./L on a chronic basis. Screening level risk assessment (acute RQ: 0.02 and chronic RQ:0.01) indicate that the proposed use of spinetoram will pose a negligible risk to marine fish on acute and chronic basis.

Marine invertebrates: On an acute basis, the NOEC and LC_{50} values for the marine crustacean (mysid shrimp) were 0.076 and 0.355 mg a.i./L, respectively. The corresponding values for eastern oyster were 0.084 and 0.393 mg a.i./L. On a chronic basis, spinetoram would adversely affect marine crustaceans at concentrations greater than 0.0194 mg a.i./L. However, screening level risk assessment (mysid shrimp acute RQ: 0.07 and chronic RQ:0.67) indicate that the proposed use of spinetoram will pose a negligible risk to these organisms on acute and chronic basis.

Marine algae: For the marine diatom, the EC_{50} was 0.086 mg a.i./L and spinetoram would adversely affect them at concentrations greater than 0.014 mg a.i./L (NOEC). However, screening level risk assessment (RQ: 0.15) indicated that the proposed use of spinetoram will pose a negligible risk to marine diatoms.

4.2.3 Tier 1 Risk Assessment: Spray Drift

Screening level risk assessment indicated that the proposed use of spinetoram would pose a chronic risk to freshwater invertebrates, benthic organisms and amphibians. A Tier 1 risk assessment was, therefore, undertaken to determine the potential for effects on sensitive aquatic organisms resulting from spray drift (Appendix I, Table 17). With a maximum cumulative application rate of 105–305 g a.i./ha and assuming a spray drift of 11% (insecticide with a fine spray quality) at one metre downwind, the drift would be 11.58 g a.i./ha. With a spray drift of 11.58 g a.i./ha, the EECs in a water body of 15 cm and 80 cm depth would be 0.008 and 0.002 mg a.i./L, respectively.

The RQ value of 0.2 indicates that drift with the use of spinetoram will pose a negligible risk to freshwater amphibians on a chronic basis. It will, however, pose a risk to freshwater invertebrates (RQ: 33.30) and benthic organisms (RQ: 1.25) on a chronic basis and, therefore, mitigatory measures are required to protect these organisms.

4.2.4 Tier 1 Risk Assessment: Run-off

A Tier 1 risk assessment was undertaken to determine the potential for effects on sensitive aquatic organisms resulting from surface run-off water from the treated areas. The EECs for spinetoram in a one hectare receiving water body, resulting from run-off, were predicted by PRZM-EXAMS (Appendix I, Table 18). The values reported by PRZM/EXAMS are 90^{th} percentile concentrations of the yearly peaks determined at a number of time-frames including the yearly peak, 96-hr, 21-d, 60-d, 90-d and yearly average.

At the screening level, risk was identified with chronic exposure to water flea, benthic organisms and amphibians. The maximum concentrations of 0.51 µg a.i./L (15 cm water depth) and 0.43 µg a.i./L (80 cm water depth) due to runoff during 21-day exposure period was, therefore, considered for risk assessment. The RQ values of 0.01 and 0.27 for amphibians and benthic organisms, respectively, indicate that the spinetoram will pose a negligible risk to these organisms. The RQ value of 7.17, however, indicates that the proposed use of spinetoram will pose a risk to fresh water invertebrates.

Environmental concerns: An environmental risk assessment with the use of spinetoram as an insecticide has identified the following concerns:

- acute risk to honey bees
- dietary risk to wild mammals
- chronic risk to freshwater invertebrates
- chronic risk to benthic organisms
- may pose a risk to predatory and parasitic arthropods

5.0 Value

5.1 Effectiveness Against Pests

Forty-five efficacy trial reports were submitted in support of registration of the active ingredient spinetoram and the two associated end-use products. Some of these reports included more than one trial or assessment of efficacy against more than one pest. Counting assessments against different pests as separate trials, 64 trials were conducted for 20 different pest species on 14 different crops. Trials were conducted in British Columbia, Ontario, Prince Edward Island, Nova Scotia, Maine, Massachusetts, New York, Pennsylvania, Indiana, Washington, California, Arizona, Texas and Mississippi in the years 2002 through 2006. Three different formulations of spinetoram were tested, including Radiant SC Insecticide, Delegate WG Insecticide and another formulation similar to Radiant SC Insecticide but containing a lower concentration of the active ingredient (100 g/L rather than 120 g/L). These products were assessed against untreated controls

and various commercial standards, including products containing spinosad as the active ingredient, and provided control that was generally similar or in some cases superior to the commercial standards used.

Label claims were supported by the submitted efficacy data or in some cases supported by extrapolation from the submitted efficacy data with consideration of pest biology and crop structure, as discussed below.

Pome Fruits

Codling moth: Efficacy trials for codling moth showed acceptable control with application rates of 100–105 g a.i./ha but showed inconsistency of control or reduced residual activity with lower application rates. Based on these efficacy data, the label claim for codling moth control was supported.

Oriental fruit moth: Efficacy trials for Oriental fruit moth on apples did not demonstrate a rate effect in most cases. The applicant proposed an application rate of 105 g a.i./ha for Oriental fruit moth based on the rationale that this pest feeds internally in the fruit, similar to codling moth, and the larger data set for codling moth indicates that lower application rates provide inconsistent control. In addition, overall application rates are similar for the products registered for use against both pests in Canada; for those products registered at different application rates, the differences are usually small and are not consistently higher or lower for one pest or the other. Due to similarity of their life cycles and the damage they cause, growers often manage these two pests together. Based on the submitted efficacy data and considering these rationales, the label claim for Oriental fruit moth control was supported.

Obliquebanded and Threelined (Pandemis) leafrollers: Application rates of 50–105 g a.i./ha produced the most consistent results for obliquebanded leafroller, with less consistent results at lower rates. Efficacy data thus supported the range of application rates, with the rate to be adjusted according to pest pressure. Life cycle and damage caused by threelined leafroller are similar to obliquebanded leafroller and therefore management of these two species of leafroller is also similar. On this basis, the label claim for obliquebanded and threelined leafroller control was supported.

Spotted and Western tentiform leafminers: Efficacy trials consistently demonstrated acceptable control of spotted tentiform leafminer with application rates of 75–100 g a.i./ha and one trial showed that efficacy of 50 g a.i./ha was comparable to the higher application rates. The label claim for control of spotted tentiform leafminer was supported. Spotted and western tentiform leafminers are closely related (congeneric), with similar life cycles and damage caused. The label claim for control of western tentiform leafminer was therefore supported by extrapolation from the submitted efficacy data for spotted tentiform leafminer.

Apple maggot: Efficacy trials indicated acceptable control of apple maggot with relatively low application rates (32 or 41 g a.i./ha)when treated apples were exposed to adult flies under laboratory conditions, but field trials indicated that control may be inconsistent with application rates of less than 100 g a.i./ha. Furthermore, application rates for apple maggot are equal to or higher than those for codling moth for all products registered for both uses in Canada. This internally-feeding pest is often difficult to control. Based on the submitted efficacy data and considering these rationales, the label claim for suppression of apple maggot was supported.

Plum curculio: Efficacy trials indicated consistent suppression of fruit damage by plum curculio at the highest application rates (100–105 g a.i./ha) but inconsistent results (0–83%) at lower application rates (≤80 g a.i./ha). These efficacy data supported the label claim for suppression of plum curculio.

Asparagus

Asparagus beetle: Application rates of 17.5, 35 and 70 g a.i./ha resulted in statistically similar reductions in defoliation. Evidence of a rate effect was not consistent; however, the range of 35–70 g a.i./ha is not excessive, combined with directions to use the higher rate under higher pest pressure and/or advanced growth stages of the beetle. These efficacy data supported the label claim for suppression of asparagus beetle.

Bushberries

Blueberry spanworm: The single efficacy trial for blueberry spanworm on lowbush blueberries demonstrated equivalent reductions in populations with application rates ranging from 26 to 105 g a.i./ha. The range of 25–50 g a.i./ha is consistent with the application rates supported for other lepidopteran pests of non-orchard crops. Furthermore, the submitted efficacy data was generated on lowbush blueberry and the higher application rate of 50 g a.i./ha may be necessary to ensure adequate coverage on highbush blueberry. The label claim for control of blueberry spanworm was supported.

Caneberries

Obliquebanded leafroller: Efficacy trials on apples demonstrated that spinetoram is effective against obliquebanded leafroller when applied at rates of 53–105 g a.i./ha in spray volumes up to 3000 L/ha. The lower range of application rates for caneberries is appropriate for the smaller volume of foliage requiring coverage and lower spray volumes of up to 1000 L/ha applied to caneberries. Based on the efficacy data submitted for obliquebanded leafroller on apples and considering relative foliage and spray volumes, the label claim for obliquebanded leafroller on caneberries was supported.

Cereals

Armyworm: No efficacy data were submitted for armyworm on cereals, but efficacy against this pest was demonstrated in one trial for armyworm on soybean. Considering foliar volumes, plant architecture and the open-feeding nature of this pest, extrapolating from soybean to cereals is acceptable. Therefore, the label claim for armyworm on cereals was supported, with application rates adjusted as described under soybean.

Cole Crops [*Brassica* Leafy Vegetables]

Diamondback moth, Cabbage looper and Imported cabbageworm: Application rates of 50, 70 or 100 g a.i./ha provided consistently acceptable control of all three pests on cabbage, including residual control for up to two weeks; results with application rates of 35 g a.i./ha or less were less consistent. The label claim for control of diamondback moth, cabbage looper and imported cabbageworm on cole crops with application rates of 35–50 g a.i./ha was supported based on the efficacy data submitted.

Fruiting Vegetables

Cabbage looper: Application rates of 50, 70 or 100 g a.i./ha provided consistently acceptable control of cabbage looper on cabbage and lettuce, including residual control for up to two weeks; results with application rates of 35 g a.i./ha or less were less consistent. Efficacy against this pest is not expected to vary among crops as long as thorough coverage of the crop is achieved. The label claim for cabbage looper on fruiting vegetables was supported by extrapolation from efficacy data for this pest on cabbage and lettuce.

Grape

Grape berry moth: Application rates of 35 and 70 g a.i./ha provided equivalent suppression of grape berry moth on grape in the single efficacy trial submitted. However, surface feeding by grape berry moth larvae is extremely limited before the larvae bore into the fruit, so the higher application rate may be required to provide a consistently effective dose. Based on the efficacy data submitted and considering the similar biology and damage of this pest compared to other tortricid pests of fruits, the application rate of 70 g a.i./ha for grape berry moth was supported. The single efficacy trial supports the claim of suppression of grape berry moth.

Leafy Vegetables

Cabbage looper: Application rates of 50, 70 or 100 g a.i./ha provided consistently good control of cabbage looper on cabbage and lettuce, including residual control for up to two weeks; results with application rates of 35 g a.i./ha or less were less consistent. The label claim for cabbage looper on leafy vegetables was supported by the efficacy data submitted.

Leaves of Root and Tuber Vegetables

Diamondback moth, Cabbage looper and Imported cabbageworm: Application rates of 50, 70 or 100 g a.i./ha provided consistently acceptable control of all three pests on cabbage, including residual control for up to two weeks; results with application rates of 35 g a.i./ha or less were less consistent. Efficacy against these pests is not expected to vary among crops as long as thorough coverage of the crop is achieved. The label claim for control of diamondback moth, cabbage looper and imported cabbageworm on leaves of root and tuber vegetables was supported by extrapolation from efficacy data for these pests on cabbage.

Root Vegetables

Diamondback moth, Cabbage looper and Imported cabbageworm: Application rates of 50, 70 or 100 g a.i./ha provided consistently acceptable control of all three pests on cabbage, including residual control for up to two weeks. Results with application rates of 35 g a.i./ha or less were less consistent. Efficacy against these pests is not expected to vary among crops as long as thorough coverage of the crop is achieved. The label claim for control of diamondback moth, cabbage looper and imported cabbageworm on root vegetables was supported by extrapolation from efficacy data for these pests on cabbage.

Soybean

Armyworm: Application rates of 13.25 to 53 g a.i./ha produced statistically equivalent results when leaves from soybean plants treated in the field were provided to armyworms under laboratory conditions. However, results with the highest application rate were numerically superior to those with the lower application rates and without confirmatory data, it is not known whether efficacy of the lowest rate would be maintained under field conditions. Comparison to other open-feeding lepidopteran larvae, such as the cabbage looper complex for which there is a larger supporting database, suggests that a minimum application rate of 25 or 35 g a.i./ha (which produced similar results for the cabbage looper complex) might be required to obtain acceptable control of armyworm in the field. An overall range of 25–50 g a.i./ha is consistent with application rates supported for other lepidopteran pests of non-orchard crops and was therefore supported.

Stone Fruits

Oriental fruit moth: Efficacy trials submitted for Oriental fruit moth on peaches showed acceptable control with application rates of 75–105 g a.i./ha; most consistently at 105 g a.i./ha. Based on the submitted efficacy data and considering the rationale for pome fruits, the label claim for control of Oriental fruit moth on stone fruits was supported.

Obliquebanded and Threelined (Pandemis) leafrollers: Application rates of 50–105 g a.i./ha produced the most consistent results for obliquebanded leafroller on apples, with less consistent results at lower rates. Life cycle and damage caused by threelined leafroller are very similar to obliquebanded leafroller and therefore management of these two species of leafroller is also very similar. Efficacy against these pests is not expected to vary among tree fruits as long as thorough coverage of the trees is achieved. On this basis, the label claim for obliquebanded and threelined leafrollers on stone fruits was supported.

Strawberry

Thrips: Efficacy trials submitted for flower thrips on strawberry tested only application rates of 25 and 50 g a.i./ha. Results with 50 g a.i./ha were significantly better than with 25 g a.i./ha; however, even the best results did not exceed 71% reduction in numbers of thrips. The range of 50–70 g a.i./ha is within the acceptable rate range and provides some flexibility to adjust for pest pressure, but the submitted efficacy data supported a claim of suppression only.

Table 5.1.1 Acceptable Efficacy Claims

Pest(s)	Crop(s)	Application Rate Per Hectare	
		Radiant SC Insecticide (mL of product)	Delegate WG Insecticide (g of product)
Codling Moth	Pome Fruit	875	420
Spotted and Western Tentiform Leafminers	Pome Fruit	440–875	210–420
Apple Maggot (suppression)	Pome Fruit	875	420
Plum Curculio (suppression)	Pome Fruit	875	420
Oriental Fruit Moth	Pome Fruit Stone Fruit	875	420
Obliquebanded and Threelined (Pandemis) Leafrollers	Pome Fruit Stone Fruit	440–875	210–420
Obliquebanded Leafroller	Caneberries	210–420	100–200
Asparagus Beetle (suppression)	Asparagus (fern)	290–580	140–280
Thrips (suppression)	Strawberry	420–580	200–280
Blueberry Spanworm (suppression)	Bushberries	210–420	100–200

Pest(s)	Crop(s)	Application Rate Per Hectare	
		Radiant SC Insecticide (mL of product)	Delegate WG Insecticide (g of product)
Armyworm	Cereals Soybean	210–420	100–200
Cabbage Looper, Diamondback Moth Imported Cabbageworm	Cole Crops (*Brassica* Leafy Vegetables) Leaves of Root and Tuber Vegetables Root Vegetables	290–420	140–200
Cabbage Looper	Fruiting Vegetables and Okra Leafy Vegetables (non-*Brassica*)	290–420	140–200
Grape Berry Moth (suppression)	Grape	580	280

5.2 Phytotoxicity to Host Plants

Of the 45 trial reports submitted, 31 included assessments of phytotoxicity: 10 on apple (5 different varieties), 6 on peach (at least 2 different varieties), 4 on cabbage, 2 each on potato (2 different varieties) and strawberry and 1 each on pear, grape, lowbush blueberry, cranberry, cucumber, onion and asparagus. These reports included trials with up to seven applications at rates up to 100 g a.i./ha. No evidence of phytotoxicity was observed in any of the trials.

5.3 Economics

No economic assessment was conducted for this product evaluation.

5.4 Sustainability

5.4.1 Survey of Alternatives

Availability of alternative insecticides varies depending on the pest and the crop, with a variety of different alternatives available for most uses. Some of the currently available alternatives are older classes of chemistry (carbamates and organophosphates), which are currently under re-evaluation. Other alternatives include botanical insecticides, synthetic pyrethroids, neonicotinoids, growth regulators, pheromones, microbials and kaolin clay.

Alternative active ingredients are listed by pest and crop in Appendix I, Table 19.

5.4.2 Compatibility with Current Management Practices Including Integrated Pest Management

Application of Radiant SC Insecticide or Delegate WG Insecticide using conventional ground application equipment to control or suppress various insect pests of various fruit, vegetable and cereal crops is compatible with current management practices, including integrated pest management. Growers are familiar with the monitoring techniques to determine if and when applications are needed.

5.4.3 Information on the Occurrence or Possible Occurrence of the Development of Resistance

Repeated use of insecticides having the same mode of action increases the probability of selecting biotypes (groups of insects within a species that have biological traits not common to the species as a whole) with less susceptibility to insecticides with the same mode of action. Therefore, products containing spinetoram should be used in rotation with insecticides that have different modes of action. The only other Group 5 Insecticide currently registered in Canada is spinosad, which is registered for some, but not all, of the same uses as spinetoram. The labels for Radiant SC Insecticide and Delegate WG Insecticide include the recommended statements for resistance management as per Regulatory Directive DIR99-06, *Voluntary Pesticide Resistance-Management Labelling Based on Target Site/Mode of Action*.

5.4.4 Contribution to Risk Reduction and Sustainability

Spinetoram is registered for use against a broader range of pests than the only other currently registered Group 5 Insecticide, spinosad. Additional pests for which spinetoram is registered include such key pests as codling moth, commonly controlled by older classes of chemistry, such as organophosphates which are under re-evaluation. Spinetoram qualifies as an organophosphate replacement. Spinetoram also provides a new mode of action for several pests which may be used in rotation to prevent the development of resistance.

6.0 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the federal government's Toxic Substances Management Policy (TSMP), which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

During the review process, spinetoram was assessed in accordance with the PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*. Substances associated with the use of spinetoram were also considered, including major transformation products formed in the environment, microcontaminants in the technical product and formulants in the end-use products, Radiant SC Insecticide and Delegate WG Insecticides. The PMRA has reached the following conclusions:

- Spinetoram does not meet the criteria for persistence. Its values for half-life in air (non-volatile), water (20 hours), soil (<1 day) and sediment (131 days) are below the TSMP Track 1 cut-off criteria for air (≥2 days), water (≥182 days), soil (≥182 days) and sediment (≥365 days).

- Spinetoram is not bioaccumulative. Studies have shown that the bioconcentration factors are 11– 430, which are below the TSMP Track 1 cut-off criterion of BCF ≥5,000; or the *n*-octanol–water partition coefficient (log K_{ow}) is 2.44–4.82, which is below the TSMP Track 1 cut-off criterion of ≥5.0.

- Spinetoram does not meet the criteria for toxicity (see Sections 3.6, 4.7 and 6.4).

- Spinetoram does not form any major transformation products that meet the TSMP Track 1 criteria.

- Spinetoram (technical grade) does not contain any by-products or microcontaminants that meet the TSMP Track 1 criteria. Impurities of toxicological concern are not expected to be present in the raw materials nor are they expected to be generated during the manufacturing process.

The formulated product does not contain any formulants that are known to contain TSMP Track 1 substances.

Therefore, the use of Radiant SC Insecticide and Delegate WG Insecticide is not expected to result in the entry of Track 1 substances into the environment.

- Technical grade Spinetoram does not contain any contaminants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

- The end-use products, Radiant SC Insecticide and Delegate WG Insecticides, do not contain any formulants of health or environmental concern identified in the *Canada Gazette*, Part II, Volume 139, Number 24, pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern*.

7.0 Summary

7.1 Human Health and Safety

In conjunction with the referenced database for spinosad, the toxicology database submitted for spinetoram is adequate to define the majority of toxic effects that may result from human exposure to spinetoram. In subchronic and chronic studies on laboratory animals, target organs included the thyroid gland, spleen, adrenals, thymus, liver, kidneys, hematopoeitic system and various lymphatic tissues. The available information suggests that spinetoram behaves in a similar manner to cationic amphiphilic drugs, resulting in the vacuolation of various lymphoid tissues. Further information in relation to the histochemical composition of the vacuoles is required to support this position. In addition, as scientific literature information suggests that lung macrophages may be more susceptible to the proposed mode of action, a repeat dose inhalation study will be required. There was no evidence of genotoxicity or neoplastic lesions in the database. There was no evidence of increased susceptibility of the young and spinetoram is not expected to be a developmental or reproductive toxicant. Spinetoram is not considered to be a neurotoxicant.

Mixer, loader, applicators and workers entering treated areas are not expected to be exposed to levels of spinetoram that will result in unacceptable risk when Radiant SC Insecticide and Delegate WG Insecticide are used according to label directions.

The nature of the residue in plants and animals is adequately understood. The residue definition is XDE-175-J, XDE-175-L, ND-J and NF-J. The use of spinetoram on crops listed on the label and the import of spinetoram treated commodities does not constitute an unacceptable chronic dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits to protect human health. The PMRA recommends that the following maximum residue limits be specified for residues of spinetoram:

MRLs (ppm)	Foods
7	Leafy *Brassica* greens (crop subgroup 5B including bok choy, Chinese cabbage, broccoli raab, collards, kale, mustard greens, mustard spinach, rape greens); Leafy vegetables (crop group 4 including amaranth, arugula, cardoon, celery, celtuce, Chinese celery, corn salad, dandelion leaves, dock, edible leaved chrysanthemum, endives, fresh chervil leaves, fresh Florence fennel leaves and stalk, garden cress, garden purslane, garland chrysanthemum, head lettuce, leaf lettuce, New Zealand spinach, orach leaves, parsley leaves, radicchio, rhubarb, spinach, Swiss chard, upland cress, vine spinach, winter purslane); leaves of root and tuber vegetables (crop group 2 including black salsify tops, cassava leaves, celeriac tops, chicory tops, edible burdock tops, garden beet tops, oriental radish tops, radish tops, rutabaga tops, tanier leaves, taro leaves, turnip tops, turnip-rooted chervil tops)
3	Citrus oil

MRLs (ppm)	Foods
2	Head and stem *Brassica* vegetables (crop subgroup 5A including broccoli, Brussels sprouts, cabbages, cauliflower, Chinese broccoli, Chinese mustard cabbage, kohlrabi, Napa Chinese cabbage).
1	Grape juice
0.7	Raisin, strawberry
0.5	Berries (crop group 13 including blackberries, blueberries, currants, elderberries, gooseberries, huckleberries, loganberries, raspberries).
0.4	Grape
0.3	Cucurbit vegetables [crop group 9 including balsam apples, balsam pears, cantaloupes, chayote fruit, Chinese cucumbers, Chinese waxgourds, citron melons, cucumbers, edible gourds (other than those listed in this item), muskmelons (other than those listed in this item), pumpkins, summer squash, watermelons, West Indian gherkins, winter squash]; edible-podded legume vegetables (crop subgroup 6A including edible-podded dwarf peas, edible-podded jackbeans, edible-podded moth beans, edible-podded peas, edible-podded pigeon peas, edible-podded runner beans, edible-podded snap beans, edible-podded snow peas, edible-podded soybeans, edible-podded sugar snap peas, edible-podded swordbeans, edible-podded wax beans, edible-podded yardlong beans); citrus (crop group 10 including calamondins, citrus citron, citrus hybrids, grapefruits, kumquats, lemons, limes, oranges, pummelos, satsuma mandarins, tangerines).
0.2	Fruiting vegetables (crop group 8 including bell peppers, eggplants, groundcherries, non-bell peppers, pepinos, pepper hybrids, tomatillos, tomatoes); okra; stone fruits (crop group 12 including apricots, nectarines, peaches, plumcots, plums, prune plums, sweet cherries, tart cherries).
0.1	Pome fruits (crop group 11 including apples, crabapples, loquats, mayhaws, oriental pears, pears, quinces); root vegetables (crop subgroups 1Aand1B including black salsify roots, carrot roots, celeriac roots, chicory roots, edible burdock roots, garden beet roots, ginseng roots, horseradish roots, oriental radish roots, parsnip roots, radish roots, rutabaga roots, salsify roots, skirret roots, Spanish salsify roots, sugar beet roots, turnip roots, turnip-rooted chervil roots, turnip-rooted parsley roots); wheat, barley, oat, rye.

MRLs (ppm)	Foods
0.04	Asparagus; corn (field, sweet, pop); cranberry; tuberous and corm vegetables (crop subgroups 1Cand1D including arracacha, arrowroot, cassava roots, chayote roots, Chinese artichokes, chufa, edible canna, ginger roots, Jerusalem artichokes, lerens, potatoes, sweet potato roots, tanier corms, taro corms, true yam tubers, turmeric roots, yam bean roots); succulent shelled pea and bean (crop subgroup 6B including succulent shelled blackeyed peas, succulent shelled broad beans, succulent shelled English peas, succulent shelled garden peas, succulent shelled green peas, succulent shelled lima beans, succulent shelled peas, succulent shelled pigeon peas, succulent shelled southern peas); dried shelled pea and bean, except soybean (crop subgroup 6C including dry adzuki beans, dry beans, dry blackeyed peas, dry broad beans, dry catjang seed, dry chickpeas, dry field peas, dry guar seed, dry kidney beans, dry lablab beans, dry lentils, dry lima beans, dry moth beans, dry mung beans, dry navy beans, dry pigeon peas, dry pink beans, dry pinto beans, dry rice beans, dry southern peas, dry tepary beans, dry urd beans, grain lupin, mung bean sprouts); soybean.
7.5	Milk, fat
5.5	Fat of cattle, goats, sheep and horses.
0.85	Liver of cattle, goats, sheep and horses.
0.6	Meat byproducts of cattle, goats, sheep and horses.
0.3	Milk
0.2	Meat of cattle, goats, sheep and horses.
0.04	Meat, meat byproducts and fat of hog and poultry, egg

7.2 Environmental Risk

The use of spinetoram will pose an acute risk to honey bees, a dietary risk to wild mammals and chronic risk to fresh water invertebrates and benthic organisms. Risk to bees and wild mammals is mitigated by the appropriate label statements. Risk to freshwater invertebrates and benthic organisms is mitigated by the environmental hazard statements and buffer zones.

7.3 Value

Spinetoram and the end-use products Radiant SC Insecticide and Delegate WG Insecticide have value in providing control or suppression of various insect pests on pome fruits, stone fruits, caneberries, blueberries, strawberry, grape, asparagus (fern), *Brassica* leafy vegetables, leaves of root and tubers, root vegetables, fruiting vegetables, leafy vegetables (non-*Brassica*), cereals and soybean. Spinetoram provides a new alternative active ingredient for uses that have traditionally relied on older classes of chemistry as well as uses that have few other registered alternatives.

7.4 Unsupported Uses

Insufficient efficacy data were provided to support use against European corn borer on corn, legume vegetables and potatoes and tuberous and corm vegetables; Colorado potato beetle on fruiting vegetables and potatoes and tuberous and corm vegetables; cucumber beetle on cucurbit vegetables and blackheaded fireworm on cranberry.

8.0 Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, has granted conditional registration for the sale and use of the technical grade active ingredient spinetoram and the end-use products Radiant SC Insecticide and Delegate WG Insecticide to control a variety of insect pests in pome fruits, asparagus, bushberries, cereals, caneberries, cole crops, fruiting vegetables, grape, leafy vegetables, root vegetables, stone fruits, soybeans and strawberries.

An evaluation of current scientific data from the applicant and information from other regulatory agencies has resulted in the determination that, under the approved conditions of use, the end-use products have value and do not present an unacceptable risk to human health or the environment.

Although the risks and value have been determined to be acceptable when all risk reduction measures are followed, as a condition of these registrations, the following additional scientific information is required as a result of this evaluation. (For more details, refer to the Section 12 Notice associated with these conditional registrations.)

- **Chemistry**

    - Analytical data from at least five batches of technical grade active ingredient representing full-scale production and a revised statement of product specification form (SPSF) are required. Validated analytical methods and confirmation of identity must be provided for all impurities.

    - Storage stability data for both end use products representing at least one year of storage at ambient conditions are required.

- **Human Health**

    Toxicology:
    - 90-day Inhalation study
    - Information identifying the contents of the vacuoles (histochemical analysis) observed in various tissues of lymphoid and endocrine systems; this requirement may be satisfied concurrently with the 90-day inhalation study
    - 2-year chronic toxicity/carcinogenicity study in rats

Food residue:

- Processing studies on orange and grape are required

- **Environment**

  - acute toxicity to *Daphnia* sp (DACO 9.3.2)
  - acute toxicity to cold water fish (DACO 9.5.2.1)

  - the modified soil and sediment analytical method which includes the O-demethyl-175-J and O-demethyl-175-L metabolites

NOTE: The PMRA will publish a consultation document at the time when there is a proposed decision on applications to convert these conditional registrations to full registrations or on applications to renew the conditional registrations, whichever occurs first.

List of Abbreviations

µg	micrograms
1/n	exponent for the Freundlich isotherm
a.i.	active ingredient
ADI	acceptable daily intake
ALS	acetolactate synthase
ARfD	acute reference dose
atm	atmosphere
BCF	bioconcentration factor
bw	body weight
CAS	chemical abstracts service
cm	centimetres
DF	dry flowable
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in the test population)
DT_{75}	dissipation time 75% (the dose required to observe a 75% decline in the test population)
EC_{10}	effective concentration on 10% of the population
EC_{25}	effective concentration on 25% of the population
ER_{25}	effective rate for 25% of the population
g	gram
ha	hectare(s)
HAFT	highest average field trial
HCT	hematocrit
HDT	highest dose tested
Hg	mercury
HGB	hemoglobin
HPLC	high performance liquid chromatography
IUPAC	International Union of Pure and Applied Chemistry
i.v.	intravenous
kg	kilogram
K_d	soil-water partition coefficient
K_F	Freundlich adsorption coefficient
km	kilometre
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOAEL	lowest observed adverse effect level
LOD	limit of detection
LOEC	low observed effect concentration
LOQ	limit of quantitation
LR_{50}	lethal rate 50%

mg	milligram
mL	millilitre
MAS	maximum average score
MOE	margin of exposure
MRL	maximum residue limit
MS	mass spectrometry
N/A	not applicable
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
NOER	no observed effect rate
N/R	not required
NZW	New Zealand white
OC	organic carbon content
OM	organic matter content
PBI	plantback interval
PHI	preharvest interval
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
RSD	relative standard deviation
RQ	risk quotient
SC	soluble concentrate
$t_{1/2}$	half-life
T3	tri-iodothyronine
T4	thyroxine
TSH	thyroid stimulating hormone
TRR	total radioactive residue
TSMP	Toxic Substances Management Policy
UAN	urea ammonium nitrate
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet
v/v	volume per volume dilution

Appendix I Tables and Figures

Table 1 Residue Analysis

Matrix	Method ID	Analyte	Method Type	LOQ	Reference PMRA #
Plant	GRM 05.03 and GRM 05.04	XDE-175-J, XDE-175-L, ND-J, ND-L, NF-J, NF-L	HPLC-MS/MS	0.01 ppm/analyte in wet crop, dry crop, acidic crop and oily crop	1096658 1096654
Animal	GRM 05.15	XDE-175-J, XDE-175-L, ND-J, ND-L, 3'-O-deethyl-175-J, 3'-O-deethyl-175-	HPLC-MS/MS	0.01 ppm/analyte in bovine (muscle, kidney, liver, fat), poultry (muscle, liver, fat), milk, cream and egg.	1096656
	GRM 06.08	XDE-175-J, XDE-175-L, ND-J, NF-J		0.01 ppm/analyte in bovine (muscle, kidney, liver, fat), poultry (muscle, liver, fat), milk, cream and egg.	1385793
Soil and Sediment	GRM 05.01	XDE-175-J	HPLC-MS/MS 748.6, 142.2 m/z	0.00387 ppm	1096488
		XDE-175-L	HPLC-MS/MS 760.9, 142.2 m/z	0.00365 ppm	1096488
		XDE-175-J-N-Demethyl-J	HPLC-MS/MS 734.9, 128.2 m/z	0.0023 ppm	1096488
		XDE-175-J-N-Demethyl-L	HPLC-MS/MS 746.7, 128.2 m/z	0.0027 ppm	1096488

Matrix	Method ID	Analyte	Method Type	LOQ		Reference PMRA #
Water	GRM 05.12	XDE-175-J	HPLC-MS/MS 748.6, 142.2 m/z	0.022 ppb	Drinking water	1096492
				0.0207 ppb	Ground water	
				0.0214 ppb	Surface water	
		XDE-175-L	HPLC-MS/MS 760.9, 142.2 m/z	0.0325 ppb	Drinking water	1096492
				0.0293 ppb	Ground water	
				0.0166 ppb	Surface water	
		XDE-175-J-N-Demethyl-J	HPLC-MS/MS 734.9, 128.2 m/z	0.0428 ppb	Drinking water	1096492
				0.0234 ppb	Ground water	
				0.0186 ppb	Surface water	
		XDE-175-J-N-Demethyl-L	HPLC-MS/MS 746.7, 128.2 m/z	0.0224 ppb	Drinking water	1096492
				0.0212 ppb	Ground water	
				0.0351 ppb	Surface water	

Table 2 Acute Toxicity of XDE-175 and Its Associated End-use Products (Radiant SC Insecticide and Delegate WG Insecticide)

Study Type	Species	Result	Comment	Reference
Acute Toxicity of XDE-175 Technical				
Oral	Rat	LD_{50} > 5000 mg/kg bw	LOW TOXICITY	1096372
Dermal	Rat	LD_{50} > 5000 mg/kg bw	LOW TOXICITY	1096374
Inhalation	Rat	LC_{50} > 5.50 mg/L	LOW TOXICITY	1096424
Skin irritation	Rabbit	MAS[a] = 0	Non-irritating	1096428
Eye irritation	Rabbit	MAS = 0	Non-irritating	1096426
Skin sensitization (LLNA)	Mouse	Positive	Potential skin sensitizer	1096430
Acute Toxicity of End-Use Product—Radiant SC Insecticide				
Oral	Rat	LD_{50} > 5000 mg/kg bw	LOW TOXICITY	1096622
Dermal	Rat	LD_{50} > 5000 mg/kg bw	LOW TOXICITY	1096624
Inhalation	Rat	LC_{50} > 5.04 mg/L	LOW TOXICITY	1096626
Skin irritation	Rabbit	MAS = 0.1	Minimally irritating	1096630
Eye irritation	Rabbit	MAS = 2	Minimally irritating	1096628

Study Type	Species	Result	Comment	Reference
Skin sensitization (LLNA)	Mouse	Negative		1096632
Acute Toxicity of End-Use Product—Delegate WG Insecticide				
Oral	Rat	LD_{50} > 5000 mg/kg bw	LOW TOXICITY	1378701
Dermal	Rat	LD_{50} > 5000 mg/kg bw	LOW TOXICITY	1378702
Inhalation	Rat	LC_{50} > 5.28 mg/L	LOW TOXICITY	1378703
Skin irritation	Rabbit	MAS = 0	Non-irritating	1378705
Eye irritation	Rabbit	MAS = 6.33	Minimally irritating	1378704
Skin sensitization (LLNA)	Mouse	Negative		1378706

[a] MAS = maximum average score for 24, 48 and 72 hours

Table 3 Toxicity Profile of Technical Spinetoram

Study Type	Species	Results[a] (mg/kg/day)	Reference
1-month dietary	Rat	NOAEL (♂): 48.4 LOAEL (♂): 185; decreased body-weight gain, food consumption; cytoplasmic vacuolation of thyroid follicular cells; aggregates of histiocytic macrophages in spleen and mesenteric lymph node; tubular epithelium vacuolation in the kidney NOAEL (♀): 11.7 LOAEL (♀): 48.2; tubular vacuolation in the kidney	1096443
1-month dietary	Mouse	NOAEL: 24.5/31.3 LOAEL: 75.1/96.3; decreased HGB and HCT (♂); cytoplasmic vacuolation of parenchymal cells epithelial cells and macrophages; vacuolation of fibroblasts of skin and subcutis; vacuolation of epithelium in epididymides (♂)	1096445
1-month dietary	Dog	NOAEL: 5.9/8.1 LOAEL: 30.9/35.1; decreased body-weight (♂); body-weight loss and decreased food consumption (♀); clinical chemistry changes; hematological changes; organ weight changes; vacuolation of macrophages in various lymphoid tissues; effects in bone marrow; hyperplasia and hypertrophy of Kupffer cells; extramedullary hematopoiesis of spleen	1096441

Study Type	Species	Results[a] (mg/kg/day)	Reference
3-month dietary with 4-week recovery	Rat	NOAEL (♂): 32.4 LOAEL (♂): 65.8; histiocytic aggregates of macrophages in various tissues; follicular epithelial vacuolation of thyroid NOAEL (♀): 9.5 LOAEL (♀): 39.6; increased incidence of kidney tubular vacuolation; histiocytic aggregates of macrophages in various lymphoid tissues; follicular epithelial vacuolation of thyroid	1096432
3-month dietary	Mouse	NOAEL (♂): not determined LOAEL (♂): 7.5; multifocal degeneration with regeneration of kidney tubules NOAEL (♀): 10.2 LOAEL (♀): 29.6; increased incidence of extramedullary hematopoiesis in the spleen.	1096435
3-month dietary	Dog	NOAEL (♂): not determined LOAEL (♂): 5.7; decreased body-weight, body-weight gain; vacuolation of macrophages in various lymphoid tissues. NOAEL (♀): 4.97 LOAEL (♀): 10.2; hematological changes; vacuolation of macrophages in various lymphoid tissues; bone marrow necrosis; extramedullary hematopoiesis in spleen and/or liver; arteritis in various tissues.	1096438
4-week dermal	Rat	NOAEL: 1000 LOAEL: > 1000; non-adverse epidermal hyperplasia and hyperkeratosis at treatment site	1096447
1-year dietary	Dog	NOAEL: 2.96/2.49 LOAEL: 5.36/5.83; increased liver weights (♂); arteritis in epididymides (♂) or thymus, thyroid, larynx, urinary bladder (♀) accompanied by necrosis of arterial wall	1358463
Carcinogenicity (2-year dietary) (spinosad)	Rat	NOAEL: 2.4/3.0 LOAEL: 9.5/12.0; increased incidence of thyroid follicular epithelial cell vacuolation	649920
Carcinogenicity (18-month dietary)	Mouse	NOAEL: 18.8/23.9 LOAEL: 37.5/46.6; decreased body-eight gain and food consumption (♀?); hyperplasia and/or chronic inflammation of glandular mucosa or submucosa of the stomach; increased incidence of aggregates of alveolar macrophages in the lungs (♀?); cytopalsmic vacuolation of epithelial cells of the epididymides (♂?).	1424875

Study Type	Species	Results[a] (mg/kg/day)	Reference
Two-generation reproduction	Rat	Parental systemic NOAEL: 10 Parental systemic LOAEL: 75; cytoplasmic vacuolation of thyroid follicular epithelial cells; decreased T4 and/or increased TSH Offspring systemic NOAEL: 75 Offspring systemic LOAEL: >75; no effects noted Reproductive NOAEL (♂): 75 Reproductive LOAEL (♂): >75; no effects noted Reproductive NOAEL (♀): 10 Reproductive LOAEL (♀): 75; dystocia and abnormal parturition; animal sacrifice due to moribund condition; increased post-implantation loss; increased incidence of late resorbing/retained fetuses	1281064
Developmental toxicity (Range-Finding)	Rat	Maternal NOAEL: 150 Maternal LOAEL: 300; decreased body-weight gain and food consumption Developmental NOAEL: 300 Developmental LOAEL: > 300; no effects noted	1096454
Developmental toxicity	Rat	Maternal NOAEL: 100 Maternal LOAEL: 300; decreased body-weight gain and food consumption Developmental NOAEL: 300 Developmental LOAEL: > 300; no effects noted	1096455
Developmental toxicity (Range-Finding)	Rabbit	Maternal NOAEL: 15.7 Maternal LOAEL: 30; sacrifice one animal due to decreased food consumption, body-weight loss, absent and/or decreased fecal output Developmental NOAEL: 64 Developmental LOAEL: > 64; no effects noted	1096457
Developmental toxicity	Rabbit	Maternal NOAEL: 10 Maternal LOAEL: 60; sacrifice one animal due to moribund condition. Decreased body-weight, body-weight gain, food consumption, fecal output; inanition; increased liver weights Developmental NOAEL: 60 Developmental LOAEL: > 60; no effects noted	1096458
Acute Neurotoxicity	Rat	NOAEL: 2000 mg/kg LOAEL: > 2000 mg/kg; no effects noted	1096472
Chronic Neurotoxicity	Rat	NOAEL: 36.7/44.3 LOAEL : >36.7/44.3; no effects noted	1441919
Reverse gene mutation assay	*Salmonella typhimurium/ E.coli*	Negative	1096460

Study Type	Species	Results[a] (mg/kg/day)	Reference
In vitro mammalian chromosomal aberration	Rat lymphocytes	Negative	1096464
In vitro forward gene mutation	Chinese hamster ovary cells	Negative	1096462
In vivo mammalian cytogenetics	Mouse micro nucleus assay	Negative	1096466
Metabolism	Rat	Factor J Absorption Rapid absorption with a blood concentration maximum at 1.4 – 2 hours. After 168 hours, total recoveries ranged from 88.1–97.1% of the administered dose. Distribution Tissue burdens minimal with the carcass exhibiting the highest concentration. Spinetoram does not appear to have a potential to accumulate in the body. Excretion The majority of Spinetoram is eliminated within 24 hours in the feces, 12 hours in the urine. The major route of excretion was the feces (77.4–89.6% of the administered dose), minor route being the urine (3.4–4.1% of the administered dose). Administration of the *N*-formyl plant metabolite exhibited similar findings to the parent compound within all groups. Metabolism Orally administered Spinetoram does not appear to show significant sex-differences in rats. There were seven identified metabolites, the largest proportion found in fecal extracts. The major route of metabolism was found to be glutathione conjugation with the parent compound, as well as with *N*-demethylated, *O*-deethylated and hydroxylated forms of the parent compound. The *N*-formyl plant metabolite was also highly metabolized, with an estimated 21–28% converted to metabolites in common with those formed by the parent compound.	1096468

Study Type	Species	Results[a] (mg/kg/day)	Reference
Metabolism	Rat	Factor L Absorption Rapid absorption with a blood concentration maximum at 1.3–3.5 hours. After 168 hours, total recoveries ranged from 90.4–94.9% of the administered dose. Distribution Tissue burdens minimal with the carcass and skin exhibiting the highest concentrations. Spinetoram does not appear to have a potential to accumulate in the body. Excretion The majority of Spinetoram is eliminated within 24 hours in the feces, 12 hours in the urine. The major route of excretion was the feces (78.5–86.7% of the administered dose), minor route being the urine (2.3–3.8% of the administered dose). Metabolism Orally administered Spinetoram does not appear to show significant sex-differences in rats. There were nine identified metabolites, the largest proportion found in fecal extracts. The major route of metabolism was found to be glutathione conjugation with the parent compound, as well as with *N*-demethylated and *O*-deethylated forms of the parent compound.	1096470

[a] Effects observed in males as well as females unless otherwise reported

Table 4 Toxicology Endpoints for Use in Health Risk Assessment for Spinetoram

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	MOE	Reference
Chronic Dietary	NOAEL = 2.49	1-year oral dog study	Increased liver weights, arteritis accompanied by necrosis of the arterial wall in various lymphoid tissues.	300	1358463
	ADI = 0.008 mg/kg bw/day				
Short-term Dermal	NOAEL = 1000	1-month dermal rat study	No systemic effects observed.	100	1096447
Intermediate-term Dermal	NOAEL = 1000	1-month dermal rat study	No systemic effects observed.	100	1096447
Short-term Inhalation	NOAEL = 4.9	90-day oral rat study (spinosad)	Vacuolation in various lymphoid tissues; clinical signs of toxicity; decreases in mean body weights and food consumption and evidence of anemia and possible liver damage.	300	649920

Exposure Scenario	Dose (mg/kg bw/day)	Study	Endpoint	MOE	Reference
Intermediate-term Inhalation	NOAEL = 2.49	1-year oral dog study	Increased liver weights, arteritis accompanied by necrosis of the arterial wall in various lymphoid tissues.	300	1358463

Table 5 Integrated Food Residue Chemistry Summary

NATURE OF THE RESIDUE IN APPLE			PMRA # 1096479	
Radiolabel Position	**^{14}C-XDE-175-J or ^{14}C-XDE-175-L uniformly labelled throughout the macrolide portion of the molecule.**			
Test site	Outdoor, treated areas were completely enclosed with plastic at the time of the test substance application. The plastic was removed after the application had dried			
Treatment	Foliar treatment			
Rate	^{14}C-XDE-175-J (1810 g a.i./ha), ^{14}C-XDE-175-L (1108 g a.i./ha)			
End-use product	Not specified			
Preharvest interval	7-day			
Matrix	**PHI (days)**	**[^{14}C]-XDE-175-J**	**[^{14}C]-XDE-175-L**	
Matrix	**PHI (days)**	**TRR (ppm)**	**TRR (ppm)**	
Apple fruit	0	0.87	0.431	
	1	1.671	0.626	
	3	1.33	0.888	
	7	1.158	0.356	
	14	1.094	0.528	
	30	0.713	0.728	
Metabolites Identified	**Major Metabolites (> 10% TRRs)**		**Minor Metabolites (< 10% TRRs)**	
Radiolabel Position	**[^{14}C]-XDE-175-J**	**[^{14}C]-XDE-175-L**	**[^{14}C]-XDE-175- J**	**[^{14}C]-XDE-175-L**
Apple fruit at 7-day PHI	XDE-175-J	none	ND-J, NF-J, C9-pseudoaglycone-175-J, 3'-O-deethyl-175-J	XDE-175-L, ND-L, NF-L

Over 88% TRRs for J-residues and over 63% TRR for L-residues were in rinses.
Three metabolic pathways are thought to be responsible for the breakdown of XDE-175-J and XDE-175-L in apples. One pathway involves changes to the N-demethyl moiety on the forosamine sugar to give the N-demethyl and N-formyl metabolites. Due to the presence of high levels of these metabolites in the 0 DAT samples, it is thought that these changes may be the result primarily of photolysis. The second pathway involves cleavage of the macrolide ring system at one or more positions, ultimately resulting in a complex residue mixture consisting of over a hundred individual components. The third pathway involved changes to the rhamnose sugar of XDE-175-J only, producing the 3-O-deethyl and C9-pseudoaglycone metabolites. All of the forosamine-altered metabolites and rhamnose-altered metabolites were subject to breakdown via the second pathway, which is the reason that the second pathway ultimately predominated in the residue profile for both test materials.

NATURE OF THE RESIDUE IN LETTUCE				**PMRA # 1096481**
Radiolabel Position	**^{14}C-XDE-175-J or ^{14}C-XDE-175-L uniformly labelled throughout the macrolide portion of the molecule.**			
Test site	Outdoor, in individual plastic pots.			
Treatment	Foliar treatment			
Rate	Multiple applications (MA): ^{14}C-XDE-175-J (300 g a.i./ha/appl. × 3), ^{14}C-XDE-175-L (100 g a.i./ha/appl. × 3) Single application (SA): ^{14}C-XDE-175-J (900 g a.i./ha/appl.), ^{14}C-XDE-175-L (300 g a.i./ha/appl)			
End-use product	not specified			
Preharvest interval	3-day			
Matrix	**PHI (days)**	**[^{14}C]-XDE-175-J**		**[^{14}C]-XDE-175-L**
Matrix	**PHI (days)**	**TRR (ppm)**		**TRR (ppm)**
Lettuce	1	50.474 (SA)		14.626 (SA)
	3	37.542 (SA) 11.173 (MA)		12.398 (SA) 2.878 (MA)
Metabolites Identified	**Major Metabolites (> 10% TRRs)**		**Minor Metabolites (< 10% TRRs)**	
Radiolabel Position	**[^{14}C]-XDE-175-J**	**[^{14}C]-XDE-175-L**	**[^{14}C]-XDE-175- J**	**[^{14}C]-XDE-175-L**
Lettuce (SA)	XDE-175-J, ND-J, NF-J	none	none	XDE-175-L, ND-L, NF-L
Lettuce (MA)	NF-J	none	XDE-175-J, ND-J	XDE-175-L, ND-L, NF-L

Two metabolic pathways are thought to be responsible for the breakdown of XDE-175-J and XDE-175-L in lettuce. One pathway involves alterations to the forosamine portion of the molecule with the N-demethyl and N-formyl metabolites being the primary components formed. Both of these metabolites as well as the parent compound are also subject to alterations by a second pathway, which is hypothesized to involve cleavage or opening of the macrolide ring system at one or more positions. The initial products or intermediates formed by this pathway are then further altered or metabolized to give a complex mixture of residues consisting of over a hundred individual components.

NATURE OF THE RESIDUE IN TURNIP				PMRA # 1096483
Radiolabel Position	**^{14}C-XDE-175-J or ^{14}C-XDE-175-L uniformly labelled throughout the macrolide portion of the molecule.**			
Test site	Outdoor, in individual plastic pots.			
Treatment	Foliar treatment			
Rate	Multiple applications (MA): ^{14}C-XDE-175-J (300 g a.i./ha/appl. × 3), ^{14}C-XDE-175-L (100 g a.i./ha/appl. × 3) Single application (SA): ^{14}C-XDE-175-J (900 g a.i./ha/appl.), ^{14}C-XDE-175-L (300 g a.i./ha/appl)			
End-use product	Not specified			
Preharvest interval	3-day			
Matrix	**PHI (days)**	**[^{14}C]-XDE-175-J**		**[^{14}C]-XDE-175-L**
Matrix	**PHI (days)**	**TRR (ppm)**		**TRR (ppm)**
Turnip top	1	8.067 (SA)		3.342 (SA)
	3	11.776 (SA) 7.220 (MA)		2.136 (SA) 2.159 (MA)
	7	7.661 (SA) 4.874 (MA)		1.982 (SA) 1.128 (MA)
Turnip root	1	0.029 (SA)		0.030 (SA)
	3	0.123 (SA) 0.030 (MA)		0.031(SA) 0.016 (MA)
	7	0.016 (SA) 0.098 (MA)		0.020 (SA) 0.015 (MA)
Metabolites Identified	**Major Metabolites (> 10% TRRs)**		**Minor Metabolites (< 10% TRRs)**	
Radiolabel Position	**[^{14}C]-XDE-175-J**	**[^{14}C]-XDE-175-L**	**[^{14}C]-XDE-175- J**	**[^{14}C]-XDE-175-L**
Turnip top (SA)	NF-J	None	XDE-175-J, ND-J	XDE-175-L, ND-L, NF-L
Turnip top (MA)	NF-J	None	XDE-175-J, ND-J, C17-pseudoaglycone-175-J, Aglycone-175-J	XDE-175-L, ND-L, NF-L
Turnip root (SA)	XDE-175-J, ND-J, NF-J	XDE-175-L	None	NF-L

Two metabolic pathways are thought to be responsible for the dissipation of the XDE-175-J and XDE-175-L residues in turnips. One pathway involves alterations to the forosamine sugar, with the N-demethyl and N-formyl metabolites being the primary components formed. Both of these metabolites as well as the parent test materials are also subject to alteration by a second pathway that is hypothesized to involve cleavage or opening of the macrolide ring system at one or more positions. Initial metabolites from the second pathway are then further altered or metabolized to give a complex mixture of residues consisting of over a hundred individual components.

CONFINED ACCUMULATION IN ROTATIONAL CROPS - radish, lettuce, wheat				**PMRA # 1096681**	
Radiolabel Position		**^{14}C-XDE-175-J or ^{14}C-XDE-175-L uniformly labelled throughout the macrolide portion of the molecule.**			
Test site		Confined outdoor plots			
Formulation used for trial		Same as plant metabolism studies			
Application rate and timing		^{14}C-XDE-175-J or ^{14}C-XDE-175-L at a rate of 405 g a.i./ha or 135 g a.i./ha, respectively. Wheat, lettuce and radish were planted at 30 days after soil being treated (PBI).			
Metabolites Identified		**Major Metabolites (> 10% TRR)**		**Minor Metabolites (< 10% TRR)**	
Matrix	**PBI (days)**	**[^{14}C]-XDE-175-J**	**[^{14}C]-XDE-175-L**	**[^{14}C]-XDE-175- J**	**[^{14}C]-XDE-175-L**
Radish (immature top)	30	XDE-175-J, combined ND-J/NF-J	None	None	None
Radish (mature top)	30	None	Not analyzed	None	Not analyzed
Lettuce (immature)	30	XDE-175-J, combined ND-J/NF-J	None	None	None
Lettuce (mature)	30	Combined ND-J/NF-J	None	None	None
Wheat hay	30	None	Not analyzed	None	Not analyzed
Wheat straw	30	None	None	None	None

Only the SPE eluant fractions containing TRRs greater than 0.01 ppm were analyzed. It was concluded that since the identified compounds or any potential metabolite in the SPE column is unknown, it is possible that the parent and/or metabolites were split across several SPE fractions and not been identified. However, the study demonstrats that TRRs in rotational crops planted 30 days after application are low. Therefore, a label restriction will be added: **Treated field may only be rotated to labelled crops**.

NATURE OF THE RESIDUE IN LAYING HEN	PMRA # 1096475
Laying hens were dosed orally once daily via balling gun for seven consecutive days with either ^{14}C-XDE-175-J or ^{14}C-XDE-175-L (corresponds to 10 ppm in feed). Hens were sacrificed 22±3 hrs after administration of the final dose.	

Matrices	% of the Administered Dose	
	[^{14}C]-XDE-175-J	[^{14}C]-XDE-175-L
Excreta	93.4	90.5
Muscle	0.12	0.26
Fat	0.66	1.48
Liver	0.2	0.34
Egg	0.42	1

Metabolites Identified	Major Metabolites (> 10% TRR)		Minor Metabolites (< 10% TRR)	
Radiolabel Position	[^{14}C]-XDE-175-J	[^{14}C]-XDE-175-L	[^{14}C]-XDE-175-J	[^{14}C]-XDE-175-L
Abdominal fat	XDE-175-J	XDE-175-L, O-demethyl-175-L	3'-O-deethyl-175-J, O-demethyl-175-J	3'-O-deethyl-175-L
Skin with fat	XDE-175-J	XDE-175-L, O-demethyl-175-L	O-demethyl-175-J	3'-O-deethyl-175-L
Muscle	XDE-175-J	XDE-175-L, O-demethyl-175-L	O-demethyl-175-J	3'-O-deethyl-175-L
Liver	XDE-175-J, 3'-O-deethyl-175-J	XDE-175-L, O-demethyl-175-L, 3'-O-deethyl-175-L	O-demethyl-175-J	ND-L
Egg	XDE-175-J	XDE-175-L, O-demethyl-175-L 3'-O-deethyl-175-L	None	None

Metabolism of XDE-175 appears to be primarily through dealkylation of the rhamnose sugar to give the O-deethyl and O-demethyl metabolites.

NATURE OF THE RESIDUE IN LACTATING GOAT	PMRA # 1096477
Two lactating goats were dosed orally once daily via balling gun for five consecutive days with either ^{14}C-XDE-175-J or ^{14}C-XDE-175-L uniformly labelled throughout the macrolide portion of the molecule (corresponds to 10 ppm in feed). The goats were euthanized 21±1 hours after administration of the final dose.	

Matrices	% of Administered Dose	
	[^{14}C]-XDE-175-J	[^{14}C]-XDE-175-L
Urine and feces	51.3	78.3
Muscle	0.02	0.02
Fat	0.28	0.15
Kidney	0.02	0.01
Liver	0.14	0.1
Milk	0.28	0.2

Metabolites Identified	Major Metabolites (> 10% TRR)		Minor Metabolites (< 10% TRR)	
Radiolabel Position	**[^{14}C]-XDE-175-J**	**[^{14}C]-XDE-175-L**	**[^{14}C]-XDE-175- J**	**[^{14}C]-XDE-175-L**
Fat	XDE-175-J	XDE-175-L	None	None
Muscle	XDE-175-J	XDE-175-L	None	None
Kidney	XDE-175-J	XDE-175-L	None	None
Liver	XDE-175-J	XDE-175-L	ND-J	ND-L
Milk	XDE-175-J	XDE-175-L	None	None

No significant metabolism of XDE-175 was observed in ruminants as the unchanged parent molecule was the primary residue component identified in all milk and tissue samples.

STORAGE STABILITY — **PMRA # 1320697**

Individual samples of lettuce leaves, sugar beet root, orange whole fruit, wheat grain and soybean grain spiked with either XDE-175-J, XDE-175-L, ND-J, ND-L, NF-J or NF-L at a level of 0.1 ppm were stored at –20°C for a duration of 12 months. XDE-175 and the metabolites were analyzed by HPLC-MS/MS. The results show that residues of XDE-175-J, XDE-175-L, ND-J, ND-L, NF-J and NF-L are stable in plant matrices (lettuce leaves, sugar beet root, orange whole fruit, wheat grain and soybean grain) for up to 12 months when stored frozen.

As samples in livestock metabolism studies and feeding study were analyzed within 6 months and 1 months, respectively, of freezer storage, freezer storage stability study in animal matrices are not required.

CROP FIELD TRIALS - Apple — **PMRA # 1281119, 1096666**

A) 5 apple trials were conducted in zones 1, 2, 5, 10 and 11 at a total trial rate of 494–509 g a.i./ha/season (1.6× proposed GAP)
B) 4 apple trials were conducted in zones 5, 5B and 11. Two rates were used: 233–239 g a.i./ha (0.76× proposed GAP) and 309–314 g a.i./ha (~1× proposed GAP).

Commodity	Total Applic. Rate (g a.i./ha)	PHI (days)	Residue Levels (ppm) Total residue of XDE-175 (XDE-175-J, XDE-175-L, ND-J and NF-J)						
			n	Min.	Max.	HAFT	Median (STMdR)	Mean (STMR)	Std. Dev.
Apple fruit	494–509	7	20	0.012	0.038	0.029	0.020	0.021	0.008
Apple fruit	233–239	7	8	0.015	0.037	0.035	0.022	0.024	0.008
Apple fruit	309–314	7	8	0.011	0.048	0.040	0.029	0.028	0.013

CROP FIELD TRIALS - Sugar beet									PMRA # 1096666
5 trials were conducted on sugar beet in zones 5, 7, 8, 10 and 11 at a total trial rate of 281 – 284 g a.i./ha/season (1.3× proposed GAP).									
Commodity	**Total Applic. Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm) Total residue of XDE-175 (XDE-175-J, XDE-175-L, ND-J and NF-J)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
Beet tops	281–284	3	10	0.166	0.595	0.587	0.383	0.383	0.141
Beet roots	281–284	3	10	<LOQ (<0.04)	<LOQ	<LOQ	<LOQ	<LOQ	--

CROP FIELD TRIALS - Leaf lettuce									PMRA # 1096666
5 trials were conducted on leaf lettuce in zones 1, 2, 3, 10 at a total trial rate of 299–310 g a.i./ha/season (2× proposed GAP)									
Commodity	**Total Applic. Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm) Total residue of XDE-175 (XDE-175-J, XDE-175-L, ND-J and NF-J)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
Leaf lettuce	299–310	1	10	0.266	1.335	1.223	0.615	0.743	0.406

CROP FIELD TRIALS - Tomato									PMRA # 1096666
5 trials were conducted on tomato in zones 1, 2, 3, 5, 10 at a total trial rate of 301–308 g a.i./ha/season (1.4× proposed GAP)									
Commodity	**Total Applic. Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm) Total residue of XDE-175 (XDE-175-J, XDE-175-L, ND-J and NF-J)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
Tomatoes	301–308	1	10	0.013	0.043	0.039	0.025	0.025	0.01

CROP FIELD TRIALS - Orange									PMRA # 1096666
5 trials were conducted on oranges in zones 3, 6, 10 at a total trial rate of 209–214 g a.i./ha/season (1× proposed U.S. GAP)									
Commodity	**Total Applic. Rate (g a.i./ha)**	**PHI (days)**	**Residue Levels (ppm) Total residue of XDE-175 (XDE-175-J, XDE-175-L, ND-J and NF-J)**						
			n	**Min.**	**Max.**	**HAFT**	**Median (STMdR)**	**Mean (STMR)**	**Std. Dev.**
Oranges	209–214	1	20	0.013	0.083	0.075	0.051	0.046	0.019

LIVESTOCK FEEDING – Dairy cattle	PMRA # 1360133

Three dairy cows were dosed with XDE-175 (XDE-175-J and XDE-175-L, 3:1) at a level of 37.85 ppm in feed for 29 days. Milk was collected twice daily. After 29 days of dosing, cows were sacrificed and samples of kidney, liver, muscle and fat were collected within 24 hours of last dosing.

Matrix	Feeding Level (ppm/d)	n	LOD	Min	Max	Median	Mean	Standard Deviation
Kidney	37.85	3	0.003	0.84	1.799	1.08	1.24	0.499
Liver	37.85	3	0.003	0.661	2.574	1.374	1.536	0.967
Muscle	37.85	3	0.003	0.442	0.555	0.51	0.503	0.057
Fat	37.85	3	0.003	11.082	16.609	14.838	14.176	2.822
Milk	37.85	3	0.003	0.803	0.945	0.944	0.897	0.082

The estimated maximum theoretical dietary burden (MTDB) are 11.896 ppm (0.31× of the feeding level used in the study) for beef cattle, 12.183 ppm (0.32× of the feeding level used in the study) for dairy cattle, 0.088 ppm for poultry and 0.028 ppm (0.0007× of the feeding level) for swine.
To be conservative, anticipated residues calculated in dairy cattle are used to set the MRLs.

Commodity	Feeding level (ppm)	Maximum Residues (ppm)*	MTDB (ppm)		Anticipated Residue (ppm)	
			Beef/Dairy	Hog	Beef/Dairy	Hog
Milk	37.85	0.945	11.896/12.183	0.028	0.3	—
Fat	37.85	16.609	11.896/12.183	0.028	5.31	0.01
Kidney	37.85	1.799	11.896/12.183	0.028	0.58	<0.01
Liver	37.85	2.574	11.896/12.183	0.028	0.82	<0.01
Muscle	37.85	0.555	11.896/12.183	0.028	0.18	<0.01

LIVESTOCK FEEDING – Laying hens	

Poultry feeding study was not submitted.
The estimated maximum theoretical dietary burden (MTDB) is 0.088 ppm for poultry. The data from the poultry metabolism study (10 ppm dosing level) is used to extrapolate the anticipated residues in poultry commodities. At 0.088 ppm MTDB level, the residues (XDE-175-J, XDE-175-L, ND-J and NF-J) in poultry meat, meat by products and eggs are all below the LOQ level (0.01 ppm/analyte).

Table 6 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

PLANT STUDIES	
RESIDUE DEFINITION FOR ENFORCEMENT **Primary crops** **Rotational crops**	XDE-175-J, XDE-175-L, ND-J and NF-J Cannot be determined.
RESIDUE DEFINITION FOR RISK ASSESSMENT **Primary crops** **Rotational crops**	XDE-175-J, XDE-175-L, ND-J and NF-J
METABOLIC PROFILE IN DIVERSE CROPS	Similar
ANIMAL STUDIES	
ANIMALS	**Ruminant**
RESIDUE DEFINITION FOR ENFORCEMENT	XDE-175-J, XDE-175-L, ND-J and NF-J
RESIDUE DEFINITION FOR RISK ASSESSMENT	Ruminant: XDE-175-J, XDE-175-L, ND-J and NF-J Poultry: XDE-175-J, XDE-175-L, ND-J, NF-J, 3'-O-deethyl-175-J, 3'-O-deethyl-175-L and O-demethyl-175-L
METABOLIC PROFILE IN ANIMALS **(goat, hen, rat)**	No significant metabolism of XDE-175 was observed in ruminants. The parent compound was also the primary residue component in all hen matrices, except liver. In hen liver, the O-deethyl and O-demethyl metabolites were also observed as major metabolites.
FAT SOLUBLE RESIDUE	Yes

DIETARY RISK FROM FOOD AND WATER			
	POPULATION	**ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)**	
		Food Only	**Food and Water**
Refined chronic non-cancer dietary risk **ADI = 0.008 mg/kg bw** **Estimated chronic drinking water concentration = 1.5 µg/L**	**All infants < 1 year**	28.3	29.6
	Children 1–2 years	65.9	66.5
	Children 3 to 5 years	48.6	49.1
	Children 6–12 years	29.1	29.4
	Youth 13–19 years	17.8	18.1
	Adults 20–49 years	16.7	17.1
	Adults 50+ years	17.5	17.9
	Total population	21.5	21.9
Refined acute dietary exposure analysis, 95th percentile **Estimated acute drinking water concentration = µg/L**	**POPULATION**	**ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)**	
		Food Only	**Food and Water**
ARfD = mg/kg bw	**Females 13–49 years**	not applicable	

Table 7 Fate and Behaviour in the Terrestrial Environment

Property	Test substance	Value	Comments
Abiotic transformation			
Hydrolysis	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	pH 5: stable pH 7: stable pH 9: t½ 158 d	Not a principle route of transformation in the environment
Phototransformation on soil	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	t½: 20.8 (L)–69.4 (J) d	Not a principle route of transformation in the environment
Biotransformation			
Biotransformation in aerobic soil	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	DT_{50}: 9–31 d DT_{50}: 3–15 d	Principle route of transformation; non-persistent to slightly persistent
Biotransformation in anaerobic soil	No data were submitted; data submitted under anaerobic sediment/water may be extrapolated to soil		

Property	Test substance	Value	Comments
Mobility			
Adsorption / desorption in soil	[^{14}C]XDE-175-J and [^{14}C]XDE-175-L	Ads K_d:10–300 Ads K_{oc}:1375–27 273	Immobile in silt loam soils and slightly to low mobility in other soils
Soil leaching	No data were submitted; these data are not required as data on adorption/ desorption were submitted		
Volatilization	No data were submitted; these data are not required as this product is non-volatile based on low values of vapour pressure and Henry law constant		
Field studies			
Field dissipation	GF-968 (EP)	DT_{50}: < 1 d	Non-persistent
		DT_{75}: 2–5 d no residues after 7–14 d	Low potential for a residue carryover
Field leaching	GF-968 (EP)	No residues beyond 15 cm soil depth	Low potential to leach and contaminate the ground water

Transformation products in the terrestrial environment

Property	Test substance	Transformation products	
		Major	**Minor**
Abiotic transformation			
Hydrolysis	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	N-demethyl-175-L (11.9%)	N-demethyl-175-J (6.7%)
Phototransformation on soil	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	None	None
Biotransformation			
Biotransformation in aerobic soil	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	N-demethyl-175-J (69.7%) N-demethyl-175-L(43.8%)	None
Field studies			
Field dissipation	GF-968 (EP)	N-demethyl-J (12.5%)	None

Table 8 Fate and Behaviour in the Aquatic Environment

Property	Test Material	Value	Comments
Abiotic transformation			
Hydrolysis	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	pH 5: stable pH 7: stable pH 9: t½: 158 d	Not a principle route of transformation
Phototransformation in water	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	t½: < 1 d	Principle route of transformation
Biotransformation			
Biotransformation in aerobic water systems	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	t½: 116–119 d t½: 124–131 d	Moderately persistent in aquatic systems under aerobic conditions
Biotransformation in anaerobic water systems	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	DT_{50}:385–416 d DT_{50}:1348–1386 d	Persistent in aquatic systems under anaerobic conditions
Bioaccumulation			
Bioaccumulation	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	BCF (high dose): Whole fish:86(J)–348(L) Edible tissue:43(J)–214(L) Non-edible tissue:103(J)–430(L)	Low potential for bioaccumulation
Field studies			
Field dissipation	GF-1587 (EP)	t½: 18.1–20.4 hours	Non-persistent in aquatic systems under field conditions

Transformation products in the aquatic environment

Property	Test Substance	Transformation products	
		Major	Minor
Abiotic transformation			
Hydrolysis	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	N-demethyl-175-L (11.9%)	N-demethyl-175-J (6.7%)
Phototransformation in water	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	N-demethyl-175-L (12.2%), Unidentified product (10.8%)	N-demethyl-175-J (6.6%)
Biotransformation			
Biotransformation in aerobic sediment/ water	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	N-demethyl-175-J (9.7%) and N-demethyl-175-L(12.9%)	O-demethyl-175-J (or isomer of)

Transformation products in the aquatic environment			
Property	**Test Substance**	**Transformation products**	
		Major	**Minor**
Biotransformation in anaerobic sediment/ water	[^{14}C]XDE-175-J [^{14}C]XDE-175-L	O-demethyl-175-J (27.3%) and O-demethyl-175-L (10.5%)	None
Field studies			
Field dissipation	GF-968 (EP)	N-demethyl-J (37.3%)	N-demethyl-175-L (5.7%)

Table 9 Transformation, Persistence and Mobility of Major Transformation Products Under Field Conditions

Transformation Product	$t_{½}$ or DT_{50}	Interpretation
Terrestrial environment		
N-demethyl-J	Terrestrial field DT_{50}: 8.5–12.3 d	Non-persistent under field conditions
	Terrestrial field DT_{75}: 400 d; 0–6% at the end of 462 d	Potential for carryover is limited
	Adsorption K_d:8–132; K_{oc}:1631–12127	Immobile in silt loam soils and slightly to low mobility in other soils
	Field leaching: no residues beyond 15cm soil depth	Low potential to leach and contaminate the ground water
Aquatic environment		
N-demethyl-175-J	DT_{50}: 31.1 h (combined N-demethyl 175-J + minor product of N-demethyl)	Non-persistent in aquatic systems under field conditions
	No residues observed in sediments	Low potential for partition into sediments

Table 10 Aquatic Ecoscenario Modelling Results (µg/L) for XDE-175

Region	Application Rate (g a.i./ha)	EEC (µg a.i./L)					
		Peak	96 hr	21 d	60 d	90 d	Yearly
15 cm water body							
BC (Okanagan)	315	1.17	0.27	0.08	0.05	0.04	0.02
BC (Coastal)	159	2.07	0.55	0.20	0.13	0.12	0.07
AB	210	5.20	1.24	0.38	0.35	0.33	0.18
MB	210	3.98	0.92	0.40	0.28	0.27	0.18
ON	315	3.58	0.90	0.39	0.27	0.25	0.16

Region	Application Rate (g a.i./ha)	EEC (µg a.i./L)					
		Peak	96 hr	21 d	60 d	90 d	Yearly
QC	315	5.55	1.35	0.51	0.36	0.33	0.26
NS	315	4.09	1.00	0.34	0.24	0.21	0.15
80 cm water body							
BC (Okanagan)	315	0.23	0.15	0.07	0.04	0.04	0.02
BC (Coastal)	159	0.47	0.32	0.16	0.12	0.11	0.07
AB	210	1.02	0.67	0.34	0.32	0.30	0.17
MB	210	0.80	0.54	0.35	0.27	0.27	0.18
ON	315	0.82	0.57	0.32	0.24	0.23	0.16
QC	315	1.14	0.80	0.43	0.33	0.31	0.26
NS	315	0.83	0.57	0.28	0.21	0.20	0.14

Table 11 Maximum EEC in Vegetation and Insects After a Direct Overspray

Matrix	EEC (mg a.i./kg fw)[a]	Fresh / dry weight ratios	EEC (mg a.i./kg dw)
Short range grass	58.11	3.3[b]	191.79
Leaves and leafy crops	30.42	11[b]	334.58
Long grass	26.61	4.4[b]	117.10
Forage crops	32.59	5.4[b]	175.99
Small insects	14.12	3.8[c]	53.66
Pods with seeds	2.91	3.9[c]	11.33
Large insects	2.42	3.8[c]	9.18
Grain and seeds	2.42	3.8[c]	9.18
Fruit	3.64	7.6[c]	27.66

[a] Based on correlations reported in Hoerger and Kenaga (1972) and Kenaga (1973)
[b] Fresh / dry weight ratios from Harris (1975)
[c] Fresh / dry weight ratios from Spector (1956)

Table 12 Maximum EEC in Diets of Birds and Mammals

Organism	Matrix	EEC (mg a.i./kg dw diet)
Bobwhite quail	30% Small insects 15% Forage crops 55% Grain	47.55
Mallard duck	30% Large insects 70% Grain	9.18
Rat	70% Short grass 20% Grain/seeds 10% Large insects	137.01
Mouse	25% Short grass 50% Grain/seeds 25% Leaves and leafy crops	136.18
Rabbit	25% Short grass 25% Leaves and leafy crops 25% Long grass 25% Forage crops	204.86

Table 13 Effects on Terrestrial Organisms

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]
Invertebrates				
Earthworm	Acute	XDE-175	mg a.i./kg NOEC: 1000 LC_{50}: >1000	Non toxic up to 1000 mg a.i./kg soil
	Chronic	XDE-175	mg a.i./kg NOEC: 18.65 LC_{50}: >18.65	No effects up to 18.65 mg a.i./kg soil
Bee	Oral	EXP60707A (EP)	µg a.i./bee LD_{50}: 0.11 NOEL: 0.066	Highly toxic
	Contact	EXP60707A (EP)	µg a.i./bee LC_{50}:0.024 NOEL: 0.0065	Highly toxic
	Brood / hive	XDE-175	NOEC: 110 g a.i./ha	
Predatory arthropod	No data were submitted			
Parasitic arthropod	No data were submitted			

Organism	Exposure	Test substance	Endpoint value	Degree of toxicity[a]
Birds				
Bobwhite quail	Acute	XDE-175	mg a.i./kg bw: LD_{50} was >2250 NOEL: 292	Practically non-toxic
	Dietary	XDE-175	mg a.i./kg dw: LC_{50}: >5790 NOEC: 1810	Practically non-toxic
	Reproduction	XDE-175	mg a.i./kg diet NOEC(dose): 1000	
Mallard duck	Acute	XDE-175	mg a.i./kg bw LD_{50} was >2250 NOEL: 2250	Practically non-toxic
	Dietary	XDE-175	mg a.i./kg dw: LC_{50}: > >5640 NOEC: 1770	Practically non-toxic
	Reproduction	XDE-175	mg a.i./kg diet NOEC: 995	
Mammals				
Rat	Acute	XDE-175	LD_{50}: >5000 mg a.i./kg bw	Non-toxic
	Dietary	XDE-175	NOEC: 120 mg a.i./kg diet	
	Reproduction	XDE-175	NOEC: 170 mg a.i./kg diet	
Mouse	Dietary	XDE-175	NOEC: 50 mg a.i./kg diet	
Vascular plants				
Vascular plant	Seedling emergence	GF-1640 (EP)	EC_{25}: >150 g a.i./ha	
	Vegetative vigour		EC_{25}: >150 g a.i./ha	

[a] Atkins et al. (1981) for bees and USEPA classification for others, where applicable

Table 14 Effects on Aquatic Organisms

Organism	Exposure	Test Substance	Endpoint Value (mg a.i./L)	Degree of Toxicity[a]
Freshwater species				
Daphnia magna	Chronic	XDE-175	EC_{50}: >0.000261 NOEC: 0.000062	
Chironomus sp (midge)	Chronic	XDE-175	Sediment mg a.i./kg(TWA): EC_{50}:0.24; NOEC: 0.0957 pore water (TWA): EC_{50}: 0.0028; NOEC: 0.0016	Adverse effects at >0.0016 mg a.i./L pore water
Bluegill sunfish	Acute	XDE-175	EC_{50}: 2.69 NOEC: <0.988	Moderately toxic
Fathead minnows	Chronic	XDE-175	NOEC: >0.186	
Freshwater alga blue-green	Acute	XDE-175	NOEC: 15.2 EC_{50}: >15.2	
Freshwater alga green alga	Acute	XDE-175	NOEC: 0.152 EC_{50}: 0.620	
Freshwater diatom	Acute	XDE-175	NOEC: 0.013 EC_{50}: 0.13	
Vascular plant	Acute	XDE-175	NOEC: 6.63 EC_{50}: >14.2	
Marine species				
Crustacean (mysid shrimp)	Acute	XDE-175	EC_{50}: 0.355 NOEC: 0.076	Highly toxic
	Chronic	XDE-175	NOEC: <0.0194	
Mollusk (eastern oyster)	Acute (shell deposition)	XDE-175	EC_{50}: 0.393 NOEC: 0.084	Highly toxic

Organism	Exposure	Test Substance	Endpoint Value (mg a.i./L)	Degree of Toxicity[a]
Sheepshead minnow	Acute	XDE-105	LC_{50}: 7.87 NOEC: 1.8	Moderately toxic
	Early life stages	XDE-175	NOEC: 1.73	
Marine diatom	Acute	XDE-175	NOEC: 0.014 EC_{50}: 0.086	Very highly toxic

[a] USEPA classification, where applicable

Table 15 Risk to Terrestrial Organisms

Organism	Exposure	Endpoint Value	EEC	RQ	Risk
Invertebrates					
Earthworm	Acute	NOEC: 1000 mg a.i./kg soil	0.12 mg a.i./kg soil	0	Negligible risk
	Chronic	NOEC: 18.65 mg a.i./kg soil	0.12 mg a.i./kg soil	0.01	Negligible risk
Bee	Contact	NOEC: 0.0073/kg a.i./ha	0.272/kg a.i./ha	37.26	Risk
Predatory arthropod	No data were submitted				
Parasitic arthropod	No data were submitted				
Birds					
Bobwhite quail	Acute	NOEL: 292 mg a.i./kg bw	DI:0.723 mg a.i./ind/d	68.2 d	Negligible risk
	Dietary	NOEC: 1810 mg a.i./kg dw	47.55 mg a.i./kg dw	0.03	Negligible risk
	Reproduction	NOEC: 1000 mg a.i./kg dw	47.55 mg a.i./kg dw	0.01	Negligible risk
Mallard duck	Acute	NOEL: 2250 mg a.i./kg bw	DI: 0.459mg a.i./ind/d	588 d	Negligible risk
	Dietary	1770 mg a.i./kg dw	9.18 mg a.i./kg dw	0.01	Negligible risk
	Reproduction	95 mg a.i./kg dw	9.18 mg a.i./kg dw	0.01	Negligible risk

Organism	Exposure	Endpoint Value	EEC	RQ	Risk
Mammals					
Rat	Acute	NOEL(1/10 of LD_{50}): 500 mg a.i./kg bw	0.551 mg a.i./ind/d	318 d	Negligible risk
	Dietary	NOEC: 120 mg a.i./kg diet	137.01 mg a.i./kg diet	1.14	Risk
	Reproduction	170 mg a.i./kg diet	137.01 mg a.i./kg diet	0.81	Negligible risk
Mouse	Dietary	50 mg a.i./kg diet	136.18 mg a.i./kg diet	2.72	Risk
Vascular plants					
Vascular plant	Seedling emergence	EC_{25}: 0.150 kg a.i./ha	0.272/kg a.i./ha	1.81	Risk
	Vegetative vigour	EC_{25}: 0.150 kg a.i./ha	0.272/kg a.i./ha	1.81	Risk

Table 16 Risk to Aquatic Organisms

Organism	Exposure	Endpoint Value mg a.i./L	[1]EEC:0.070 [2]EEC:0.013	RQ	Risk
Freshwater species					
Water flea	Chronic	NOEC: 0.00006	0.013	217	Risk
Bluegill sunfish	Acute	LC_{50}: 2.68	0.013	0.05	Negligible risk
Fathead minnow	Chronic	NOEC: 0.186	0.013	0.07	Negligible risk
Amphibians	Acute	[1]LC_{50}: 2.68	0.07	0.26	Negligible risk
	Chronic	[1]NOEC: 0.0406	0.07	1.72	Risk
Benthic organisms (midge)	Chronic	water NOEC: 0.0016	0.013	8.13	Risk
Freshwater diatom	Acute	EC_{50}: 0.13	0.013	0.1	Negligible risk
Vascular plant	Acute	EC_{50}: 14.2	0.013	0.002	Negligible risk

Organism	Exposure	Endpoint Value mg a.i./L	[1]EEC:0.070 [2]EEC:0.013	RQ	Risk
Marine species					
Crustacean (mysid shrimp)	Acute	LC_{50}: 0.355	0.013	0.07	Negligible risk
	Chronic	NOEC: 0.0194	0.013	0.67	Negligible risk
Mollusk (eastern oyster)	Acute	LC_{50}: 0.393	0.013	0.66	Negligible risk
Sheepshead minnow	Acute	LC_{50}: 7.87	0.013	0.02	Negligible risk
	Chronic	NOEC: 1.73	0.013	0.01	Negligible risk
Marine diatom	Acute	EC_{50}: 0.086	0.013	0.15	Negligible risk

Note: All the toxicity concentrations and EECs are mg a.i./L
[1] EEC in 15 cm water depth (amphibians)
[2] EEC in 80 cm water depth (fish and other organisms)
[4] Toxicity end point of fish were used as a surrogate for amphibian RA
Aquatic invertebrates, algae and plants (acute): RQ = EEC/(EC_{50} ÷ 2)
All other aquatic organisms: EEC/(LC_{50} ÷ 10)
Chronic risk: NOEC

Table 17 Risk to Aquatic Organisms: Tier 1 Spray Drift

Organism	Exposure	Endpoint Value mg a.i./L	[1]EEC:0.008 [2]EEC:0.002	RQ	Risk
Freshwater species					
Water flea	Chronic	NOEC: 0.00006	0.002	33.3	Risk
Amphibians	Chronic	[3]NOEC: 0.0406	0.008	0.2	Negligible risk
Benthic organisms	Chronic	Water NOEC: 0.0016	0.002	1.25	Risk

Note: All the toxicity concentrations and EECs are mg a.i./L
[1] EEC in 15 cm water depth (amphibians)
[2] EEC in 80 cm water depth (fish and other organisms)
[3] Toxicity end point of fish were used as a surrogate for amphibian RA

Table 18 Risk to Aquatic Organisms: Tier 1 Run-off

Organism	Exposure	Endpoint Value mg a.i./L	[1]EEC:0.00051 [2]EEC:0.00043	RQ	Risk
Freshwater species					
Water flea	Chronic	NOEC:0.00006	0.00043	7.17	Risk
Amphibians	Chronic	[3]NOEC:0.0406	0.00051	0.01	Negligible risk
Benthic organisms	Chronic	Water NOEC:0.0016	0.00043	0.27	Negligible risk

Note: All the toxicity concentrations and EECs are mg a.i./L
[1]: EEC in 15 cm water depth
[2]: EEC in 80 cm water depth
[3]: Toxicity end point of fish were used as a surrogate for amphibian RA
Aquatic invertebrates, algae and plants: RQ = EEC/(EC_{50} ÷ 2)
All other aquatic organisms: EEC/(LC_{50} ÷ 10)

Table 19 Alternative Insecticides for Supported Uses of Spinetoram

Pest[1]	Crop[2]	Alternative Insecticide Active Ingredients
Codling Moth	Pome Fruit	Carbaryl, Methomyl, Azinphos-methyl, Diazinon, Malathion, Phosalone, Phosmet, Endosulfan, Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin, Acetamiprid, Thiacloprid, Methoxyfenozide, Tebufenozide, Codling Moth Pheromone, *Cydia pomonella* Granulovirus, Kaolin Clay
Apple Maggot	Pome Fruit	Carbaryl, Azinphos-methyl, Diazinon, Phosalone, Phosmet, Cypermethrin, Permethrin, Thiacloprid, Kaolin Clay
Plum Curculio	Pome Fruit	Carbaryl, Azinphos-methyl, Malathion, Phosalone, Phosmet, Lambda-cyhalothrin, Cypermethrin, Permethrin, Thiacloprid, Thiamethoxam, Kaolin Clay
Spotted Tentiform Leafminer	Pome Fruit	Carbaryl, Methomyl, Oxamyl, Diazinon, Phosmet, Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin, Acetamiprid, Imidacloprid, Thiacloprid, Thiamethoxam, Abamectin, Methoxyfenozide, Tebufenozide
Western Tentiform Leafminer	Pome Fruit	Carbaryl, Cypermethrin, Permethrin, Acetamiprid, Imidacloprid, Methoxyfenozide
Oriental Fruit Moth	Pome Fruit	Acetamiprid, Thiacloprid, Methoxyfenozide, Oriental Fruit Moth Pheromone, Kaolin Clay
Oriental Fruit Moth	Stone Fruit	Carbaryl, Azinphos-methyl, Chlorpyrifos, Malathion, Phosalone, Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin, Oriental Fruit Moth Pheromone
Obliquebanded Leafroller	Pome Fruit	Carbaryl, Azinphos-methyl, Malathion, Cypermethrin, Permethrin, Spinosad, Methoxyfenozide, Tebufenozide, Leafroller Pheromone, *Bacillus thuringiensis* subsp. *kurstaki*, Kaolin Clay
Obliquebanded Leafroller	Stone Fruit	Carbaryl, Azinphos-methyl, Malathion, Spinosad, Leafroller Pheromone, *Bacillus thuringiensis* subsp. *kurstaki*

Pest[1]	Crop[2]	Alternative Insecticide Active Ingredients
Obliquebanded Leafroller	Caneberries	Carbaryl, Malathion, Rotenone, *Bacillus thuringiensis* subsp. *kurstaki*
Threelined (Pandemis) Leafroller	Pome Fruit	Carbaryl, Malathion, Cypermethrin, Permethrin, Spinosad, Methoxyfenozide, Tebufenozide, Leafroller Pheromone, *Bacillus thuringiensis* subsp. *kurstaki*, Kaolin Clay
Threelined (Pandemis) Leafroller	Stone Fruit	Carbaryl, Malathion, Spinosad, Leafroller Pheromone, *Bacillus thuringiensis* subsp. *kurstaki*
Asparagus Beetle	Asparagus	Carbaryl, Malathion, Rotenone, Pyrethrins, Cypermethrin, Deltamethrin, Potassium Salts of Fatty Acids
Blueberry Spanworm	Bushberries	Phosmet, Trichlorfon
Armyworm	Cereals	Carbaryl, Methomyl, Chlorpyrifos, Malathion, Trichlorfon
Armyworm	Soybean	
Cabbage Looper	Cole Crops	Carbaryl, Methomyl, Acephate, Malathion, Methamidophos, Naled, Endosulfan, Rotenone, Pyrethrins, Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin, Spinosad, *Bacillus thuringiensis* subsp. *kurstaki*, Diatomaceous Earth
Cabbage Looper	Fruiting Vegetables	Malathion, Rotenone, Pyrethrins, Spinosad, Tebufenozide, *Bacillus thuringiensis* subsp. *kurstaki*
Cabbage Looper	Leafy Vegetables	Carbaryl, Methomyl, Acephate, Malathion, Methamidophos, Endosulfan, Rotenone, Pyrethrins, Lambda-cyhalothrin, Spinosad, Tebufenozide, *Bacillus thuringiensis* subsp. *kurstaki*
Cabbage Looper	Leaves of Root and Tuber Vegetables	Rotenone, *Bacillus thuringiensis* subsp. *kurstaki*
Cabbage Looper	Root Vegetables	Carbaryl, Malathion, Endosulfan, Rotenone, Pyrethrins, Spinosad
Diamondback Moth	Cole Crops	Carbaryl, Methomyl, Acephate, Methamidophos, Naled, Endosulfan, Rotenone, Pyrethrins, Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin, Spinosad, *Bacillus thuringiensis* subsp. *kurstaki*, Diatomaceous Earth
Diamondback Moth	Leaves of Root and Tuber Vegetables	Rotenone, *Bacillus thuringiensis* subsp. *kurstaki*
Diamondback Moth	Root Vegetables	Carbaryl, Endosulfan, Rotenone, Pyrethrins, Spinosad

Pest[1]	Crop[2]	Alternative Insecticide Active Ingredients
Imported Cabbageworm	Cole Crops	Carbaryl, Methomyl, Acephate, Malathion, Methamidophos, Naled, Endosulfan, Rotenone, Pyrethrins, Lambda-cyhalothrin, Cypermethrin, Deltamethrin, Permethrin, Spinosad, *Bacillus thuringiensis* subsp. *kurstaki*, Diatomaceous Earth
Imported Cabbageworm	Leaves of Root and Tuber Vegetables	Rotenone, *Bacillus thuringiensis* subsp. *kurstaki*
Imported Cabbageworm	Root Vegetables	Carbaryl, Malathion, Endosulfan, Rotenone, Pyrethrins, Spinosad
Grape Berry Moth	Grape	Carbaryl, Azinphos-methyl, Diazinon, Phosalone, Phosmet, Cypermethrin, Permethrin, Spinosad, Grape Berry Moth Pheromone
Thrips	Strawberry	Rotenone

[1] Considered to be included in general claims, such as "leafrollers".

[2] May be registered only for specific crops within the indicated crop group.

Table 20 Unsupported Label Claims Proposed by Applicant

Pest(s)	Crop(s)	Rationale for Not Supporting Label Claim
Thrips	Bulb Vegetables	No residue data available.
European Corn Borer	Corn Legume Vegetables Potatoes and Tuberous and Corm Vegetables	Data insufficient to support use on potatoes or extrapolation to other crops.
Blackheaded Fireworm (suppression)	Cranberry	Data insufficient to demonstrate efficacy.
Cucumber Beetle (suppression)	Cucurbits	Data insufficient to support use on cucurbits.
Colorado Potato Beetle	Fruiting Vegetables and Okra Potatoes and Tuberous and Corm Vegetables	Data insufficient to support use on potatoes or extrapolation to other crops.
Cabbage Looper	Herbs Mint	No residue data available.
Diamonback Moth Imported Cabbageworm	Leafy Vegetables (non-*Brassica*)	Diamondback moth and imported cabbageworm are not pests of non-*Brassica* leafy vegetables.

Appendix II Supplemental Maximum Residue Limit Information—International Situation and Trade Implications

Thirty-seven of the specified Canadian MRLs are the same as those in the U.S. In some cases the MRL differs from the tolerance established in the U.S. www.access.gpo.gov/nara/cfr/waisidx_06/40cfr180_06.html:

Table 1 Differences Between MRLs in Canada and in Other Jurisdictions

Commodity	Canada (ppm)	U.S. (ppm)	Codex* (ppm)
Vegetable, root and tuber, group 1	0.04 (subgroups 1C & 1D) 0.10 (subgroups 1A & 1B)	0.1	Not reviewed by Codex
Turnip greens	7	10	
Beet greens	7	10	
Vegetable, leafy, except *Brassica*, group 4	7	8	
Brassica, leafy greens, subgroup 5B	7	10	
Vegetable, fruiting, group 8	0.2	0.4	
Okra	0.2	0.4	
Fruit, pome, group 11	0.1	0.2	
Caneberry subgroup (crop subgroup 13-07A)	0.5	0.7	
Bushberry subgroup (crop subgroup 13-07B) (except lingonberry; cranberry, highbush)	0.5	0.25	
Grain, cereal, group 15, except rice, sorghum, pearl millet, and proso millet	0.1 (wheat, barley, oat, rye)	0.04	
Small fruit vine climbing subgroup except fuzzy kiwifruit (crop subgroup 13-07F) (except gooseberry)	0.4	--	
Grape (included in subgroup 13-07F)	0.4	0.5	
Grape juice	1		
Low growing berry subgroup (crop subgroup 13-07G) (except blueberry, lowbush; cranberry)	0.7	--	
Strawberry	--	1	
Hog, fat	0.04	0.4	
Poultry, fat	0.04	0.1	

* Codex is an international organization under the auspices of the United Nations that develops international food standards, including MRLs.

MRLs may vary from one country to another for a number of reasons, including differences in pesticide use patterns and the locations of the field crop trials used to generate residue chemistry data. For animal commodities, differences in MRLs can be due to different livestock feed items and practices.

Under the North American Free Trade Agreement (NAFTA), Canada, the United States and Mexico are committed to resolving MRL discrepancies to the broadest extent possible. Harmonization will standardize the protection of human health across North America and promote the free trade of safe food products. Until harmonization is achieved, the Canadian MRLs specified in this document are necessary. The differences in MRLs outlined above are not expected to impact businesses negatively or adversely affect international competitiveness of Canadian firms or to negatively affect any regions of Canada.

Appendix III Crop Groups: Numbers and Definitions

Crop Group Number	Name of the Crop Group	Commodity
1A	Root Vegetables	black salsify roots, carrot roots, celeriac roots, chicory roots, edible burdock roots, garden beet roots, ginseng roots, horseradish roots, oriental radish roots, parsnip roots, radish roots, rutabaga roots, salsify roots, skirret roots, Spanish salsify roots, sugar beet roots, turnip roots, turnip-rooted chervil roots, turnip-rooted parsley roots
1B	Root Vegetables, except sugar beet	black salsify roots, carrot roots, celeriac roots, chicory roots, edible burdock roots, garden beet roots, ginseng roots, horseradish roots, oriental radish roots, parsnip roots, radish roots, rutabaga roots, salsify roots, skirret roots, Spanish salsify roots, turnip roots, turnip-rooted chervil roots, turnip-rooted parsley roots
1C	Tuberous and Corm Vegetables	arracacha, arrowroot, cassava roots, chayote roots, Chinese artichokes, chufa, edible canna, ginger roots, Jerusalem artichokes, lerens, potatoes, sweet potato roots, tanier corms, taro corms, true yam tubers, turmeric roots, yam bean roots.
1D	Tuberous and Corm Vegetables except potato	arracacha, arrowroot, cassava roots, chayote roots, Chinese artichokes, chufa, edible canna, ginger roots, Jerusalem artichokes, lerens, sweet potato roots, tanier corms, taro corms, true yam tubers, turmeric roots, yam bean roots.
2	Leaves of Root and Tuber Vegetables	black salsify tops, cassava leaves, celeriac tops, chicory tops, edible burdock tops, garden beet tops, oriental radish tops, radish tops, rutabaga tops, sugar beet tops, tanier leaves, taro leaves, turnip tops, turnip-rooted chervil tops.
4	Leafy Vegetables except Brassica	amaranth, arugula, cardoon, celery, celtuce, Chinese celery, corn salad, dandelion leaves, dock, edible leaved chrysanthemum, endives, fresh chervil leaves, fresh Florence fennel leaves and stalk, garden cress, garden purslane, garland chrysanthemum, head lettuce, leaf lettuce, New Zealand spinach, orach leaves, parsley leaves, radicchio, rhubarb, spinach, Swiss chard, upland cress, vine spinach, winter purslane.
0.2083333333	Head and Stem Brassica Vegetables	broccoli, Brussels sprouts, cabbages, cauliflower, Chinese broccoli, Chinese mustard, cabbage, kohlrabi, Napa Chinese cabbage.
5B	Leafy Brassica Greens	bok choy Chinese cabbage, broccoli raab, collards, kale, mustard greens, mustard spinach, rape greens.
6A	Edible-podded Legume Vegetables	edible-podded dwarf peas, edible-podded jackbeans, edible-podded moth beans, edible-podded peas, edible-podded pigeon peas, edible-podded runner beans, edible-podded snap beans, edible-podded snow peas, edible-podded soybeans, edible-podded sugar snap peas, edible-podded swordbeans, edible-podded wax beans, edible-podded yardlong beans.
6B	Succulent Shelled Pea and Bean	succulent shelled blackeyed peas, succulent shelled broad beans, succulent shelled English peas, succulent shelled garden peas, succulent shelled green peas, succulent shelled lima beans, succulent shelled peas, succulent shelled pigeon peas, succulent shelled southern peas.
6C	Dried Shelled Pea and Bean, except soybean	dry adzuki beans, dry beans, dry blackeyed peas, dry broad beans, dry catjang seed, dry chickpeas, dry field peas, dry guar seed, dry kidney beans, dry lablab beans, dry lentils, dry lima beans, dry moth beans, dry mung beans, dry navy beans, dry pigeon peas, dry pink beans, dry pinto beans, dry rice beans, dry southern peas, dry tepary beans, dry urd beans, grain lupin, mung bean sprouts.
8	Fruiting Vegetables	bell peppers, eggplants, groundcherries, non-bell peppers, pepinos, pepper hybrids, tomatillos, tomatoes.

Crop Group Number	Name of the Crop Group	Commodity
9	Cucurbit Vegetables	balsam apples, balsam pears, cantaloupes, chayote fruit, Chinese cucumbers, Chinese waxgourds, citron melons, cucumbers, edible gourds (other than those listed in this item), muskmelons (other than those listed in this item), pumpkins, summer squash, watermelons, West Indian gherkins, winter squash.
10	Citrus	calamondins, citrus citron, citrus hybrids, grapefruits, kumquats, lemons, limes, oranges, pummelos, satsuma mandarins, tangerines
11	Pome fruits	apples, crabapples, loquats, mayhaws, oriental pears, pears, quinces.
12	Stone fruits	apricots, nectarines, peaches, plumcots, plums, prune plums, sweet cherries, tart cherries.
13-07A	Caneberry subgroup	blackberry; loganberry; raspberry, red and black; wild raspberry; cultivars, varieties, and/or hybrids of these.
13-07B	Bushberry subgroup	Aronia berry; blueberry, highbush; blueberry, lowbush; buffalo currant; Chilean guava; currant, black; currant, red; elderberry; European, barberry; gooseberry; cranberry, highbush; honeysuckle, edible; huckleberry; jostaberry; Juneberry; lingonberry; native currant; salal; sea buckthorn; cultivars, varieties, and/or hybrids of these.
13-07F	Small fruit vine climbing subgroup except fuzzy kiwifruit	Amur river grape; gooseberry; grape; kiwifruit, hardy; Maypop; schisandra berry; cultivars, varieties, and/or hybrids of these.
13-07G	Low growing berry subgroup	bearberry; bilberry; blueberry, lowbush; cloudberry; cranberry; lingonberry; muntries; partridgeberry; strawberry; cultivars, varieties, and/or hybrids of these.

References

A. LIST OF STUDIES/INFORMATION SUBMITTED BY APPLICANT

1.0 The Active Ingredient, Its Properties and Uses

XDE-175 Technical Insecticide:

PMRA Document Number	Reference
1096363	2005, Chemistry Requirements for the Registration of a Technical Grade Active Ingredient (TGAI) or an Integrated System Product, N/A, MRID: N/A, DACO: 2.1,2.2,2.3,2.4,2.5,2.6,2.7,2.8,2.9
1096364	2005, Group A - Product Identity and Composition, Description of Materials Used to Produce the Product, Description of Production Process, Discussion of Formation of Impurities, Preliminary Analysis, Certified Limits, and Enforcement Analytical Method for
1096366	2005, Analytical Method and Validation for the Determination of XDE-175 in XDE-175 Technical, DAS-AM-05-012, MRID: N/A, DACO: 2.13.1
1096367	2005, Confirmation of Identitity, N/A, MRID: N/A, DACO: 2.13.2
1096368	2005, Analysis of Product Samples for Active Ingredient and Impurities in Technical Grade XDE-175 from Lab Scale Production, FOR-05-029, MRID: N/A, DACO: 2.13.3
1096369	2005, Group B: Physical and Chemical Properties of XDE-175, NAFST-05-142, MRID: N/A, DACO: 2.14.1,2.14.10,2.14.11,2.14.12,2.14.13,2.14.14,2.14.2,2.14.3,2.14.4,2.14.5,2.14.6,2.14.7,2.14.8,2.14.9
1096488	2005, Method Validation Report for the Determination of XDE-175 and its Metabolites in Soil and Sediment using Dow AgroSciences Methods GRM 05.01 and GRM 05.02, 041020, MRID: N/A, DACO: 8.2.2.1
1096489	2005, Study Profile Template (SPT) for Method Validation Report for the Determination of XDE-175 and its Metabolites in Soil and Sediment using Dow AgroSciences Methods GRM 05.01 and GRM 05.02, 041020, MRID: N/A, DACO: 8.2.2.1
1096490	2005, Independent Laboratory Validation of Dow AgroSciences Method GRM 05.02 - Determination of Residues of XDE-175 and its Metabolites in Soil and Sediment by On-Line Solid Phase Extraction and Liquid Chromatography with Tandem Mass Spectrometry, GHB-P 1

1096491 2005, Refer to 8.2.2.1 TGAI Product Submission; Method Validation Report for the Determination of XDE-175 and its Metabolites in Soil Sediment using Dow AgroSciences Methods GRM 05.01 and GRM 05.02. Study 041020, 050036, MRID: N/A, DACO: 8.2.2.2

1096492 2005, Method Validation Report for the Determination of XDE-175 and its Metabolites in Water Using Dow AgroSciences Method GRM 05.12, 051017, MRID: N/A, DACO: 8.2.2.3

1096493 2005, Method Validation Report for the Determination of XDE-175 and its Metabolites in Water Using Dow AgroSciences Method GRM 05.12, 051017, MRID: N/A, DACO: 8.2.2.3

1096494 2005, Independent Laboratory Validation of Dow AgroSciences LLC Method GRM 05.12 - Determination of Residues of XDE-175 and its Metabolites in Water by Liquid Chromatography with Tandem Mass Spectrometry, P 865 G, MRID: N/A, DACO: 8.2.2.3

Radiant SC Insecticide:

PMRA Document Number	Reference
1096619	2005, Storage Stability and Package Corrosion Characteristics of GF-1587; Accelerated Study. Interim Report - 8 Weeks Accelerated Active Ingredient Stability, Physical Stability (as it relates to test substance physical state) and Package Corrosion, FO
1096620	2005, Dielectric Breakdown Voltage - GF-1587 SC, N/A, MRID: N/A, DACO: 3.5.15
1096668	2005, Product Identification - GF-1587, N/A, MRID: N/A, DACO: 3.1.1,3.1.2,3.1.3,3.1.4
1096669	2005, Group A - Product Identity, Composition and Analysis for XDE-175 120 SC: and End-Use Product Containing XDE-175., NAFST-05-143, MRID: N/A, DACO: 3.2.1,3.2.2,3.3.1
1096670	2005, Group A - Product Identity, Composition and Analysis for XDE-175 120 SC: and End-Use Product Containing XDE-175., NAFST-05-145, MRID: N/A, DACO: 3.2.1,3.2.2,3.3.1
1096671	2005, Group A - Product Identity, Composition and Analysis for XDE-175 Water Dispersible Granule, an End-Use Product, NAFST-05-141, MRID: N/A, DACO: 3.2.1,3.2.2,3.2.3,3.3.1
1096672	2005, Group A - Product Identity, Composition and Analysis for XDE-175 Water Dispersible Granule, an End-Use Product, NAFST-05-146, MRID: N/A, DACO: 3.2.1,3.2.2,3.2.3,3.3.1

1096673 2005, Statement of Product Specification - GF-1587 SC, N/A, MRID: N/A, DACO: 3.3.2

1096674 2005, Analytical Method and Validation for the Determination of XDE-175 in GF-1587, GF-1629, and GF-1640 Formulations, DAS-AM-05-007, MRID: N/A, DACO: 3.4.1

1096675 2005, Determination of Color, Physical State, Odor, Oxidizing and Reducing Action, Flammability, Explodability, pH, Viscosity and Density of GF-1587, an End-Use Product Containing XDE-175, FAPC-052-005, MRID: N/A, DACO: 3.5.1,3.5.11,3.5.12,3.5.2,3.5.3,3.5

1096676 2005, Container Material and Description - GF-1587 SC, N/A, MRID: N/A, DACO: 3.5.5

1096677 2005, Storage Stability and Package Corrosion Characteristics of GF-1587: Accelerated Study Interim Report - 8 Week Accelerated Active Ingredient Stability, Physical Stability (as it relates to test substance physical state) and Package Corrosion., FOR-

1096678 2005, Storage Stability Data, FOR-05-022, MRID: N/A, DACO: 3.5.10

1096679 2005, Miscibility - GF-1587 SC, N/A, MRID: N/A, DACO: 3.5.13

Delegate WG Insecticide:

PMRA Document Number	Reference
1096674	2005, Analytical Method and Validation for the Determination of XDE-175 in GF-1587, GF-1629, and GF-1640 Formulations, DAS-AM-05-007, MRID: N/A, DACO: 3.4.1
1096761	2005, Product Identification - GF-1640, N/A, MRID: N/A, DACO: 3.1.1,3.1.2,3.1.3,3.1.4
1096762	2005, Group A - Product Identity, Composition and Analysis for XDE-175 Water Dispersible Granule, an End-Use Product, NAFST-05-141, MRID: N/A, DACO: 3.2.1,3.2.2,3.2.3,3.3.1
1096763	2005, Group A - Product Identity, Composition and Analysis for XDE-175 Water Dispersible Granule, an End-Use Product, NAFST-05-146, MRID: N/A, DACO: 3.2.1,3.2.2,3.2.3,3.3.1
1096764	2005, Statement of Product Specification - GF-1640 WG, N/A, MRID: N/A, DACO: 3.3.2

1096766 2005, Determination of Color, Physical State, Odor, Oxidizing an dReducing Action, Explodability, pH, and Density of GF-1640, an End-Use Product Containing XDE-175, FAPC-052-007, MRID: N/A, DACO: 3.5.1,3.5.11,3.5.12,3.5.2,3.5.3,3.5.4,3.5.6,3.5.7,3.5.8,3.5

1096767 2005, Container Material and Description - GF-1640 WG, N/A, MRID: N/A, DACO: 3.5.5

1096768 2005, Two Week Accelerated Storage Stability of GF-1640 in Glass, FOR-05-047, MRID: N/A, DACO: 3.5.10

1096769 2005, Storage Stability Data, FOR-05-047, MRID: N/A, DACO: 3.5.10

1096770 2005, Miscibility - GF-1640 WG, N/A, MRID: N/A, DACO: 3.5.13

1096771 2005, Two Week Accelerated Storage Stability of GF-1640 in Glass, FOR-05-047, MRID: N/A, DACO: 3.5.14

1096772 2005, Dielectric Breakdown, N/A, MRID: N/A, DACO: 3.5.15

2.0 Impact on Human and Animal Health

Toxicology

PMRA #	Reference

1096371 2005, Mammalian Toxicology Summaries - XDE-175 TGAI, N/A, MRID: N/A, DACO: 4.1

1096372 2005, XDE-175: Acute Oral Toxicity Study in F344/DUCRL Rats (Up-Down Procedure), 051040, MRID: N/A, DACO: 4.2.1

1096373 2005, XDE-175: Acute Oral Toxicity Study in F344/DUCRL Rats (Up-Down Procedure), 051040.SPT, MRID: N/A, DACO: 4.2.1

1096374 2005, XDE-175: Acute Dermal Toxicity Study in F344/DUCRL Rats, 051041, MRID: N/A, DACO: 4.2.2

1096423 2005, Study Profile Template (SPT) for XDE-175: Acute Dermal Toxicity Study in F344/DUCRL Rats, 051041.SPT, MRID: N/A, DACO: 4.2.2

1096424 2005, XDE-175: Acute Dust Aerosol Inhalation Toxicity Study in F344/DUCRL Rats, 051021, MRID: N/A, DACO: 4.2.3

1096425 2005, Study Profile Template (SPT) for XDE-175: Acute Dust Aerosol Inhalation Toxicity Study in F344/DUCRL Rats, 051021.SPT, MRID: N/A, DACO: 4.2.3

1096426 2005, XDE-175: Acute Eye Irritation Study in New Zealand White Rabbits, 051043, MRID: N/A, DACO: 4.2.4

1096427 2005, Study Profile Template (SPT) for XDE-175: Acute Eye Irritation Study in New Zealand White Rabbits, 051043.SPT, MRID: N/A, DACO: 4.2.4

1096428 2005, XDE-175: Acute Dermal Irritation Study in New Zealand White Rabbits, 051042, MRID: N/A, DACO: 4.2.5

1096429 2005, Study Profile Template (SPT) for XDE-175: Acute Dermal Irritation Study in New Zealand White Rabbits, 051042.SPT, MRID: N/A, DACO: 4.2.5

1096430 2005, XDE-174: Local Lymph Node Assay in BALB/cAnNCrl Mice, 051023, MRID: N/A, DACO: 4.2.6

1096431 2005, Study Profile Template (SPT) for XDE-174: Local Lymph Node Assay in BALB/cAnNCrl Mice, 051023.SPT, MRID: N/A, DACO: 4.2.6

1096432 2005, XDE-175: 90-Day Dietary Toxicity Study with a 4-Week Recovery in Fischer 344 Rats, 041029, MRID: N/A, DACO: 4.3.1

1096434 2005, Study Profile Template (SPT) for XDE-175: 90-Day Dietary Toxicity Study with a 4-Week Recovery in Fischer 344 Rats, 041029.SPT, MRID: N/A, DACO: 4.3.1

1096435 2005, XDE-175: 90-Day Dietary Toxicity Study in Crl:CD-1(ICR) Mice, 041045, MRID: N/A, DACO: 4.3.1

1096436 2005, Study Profile Template (SPT) for XDE-175: 90-Day Dietary Toxicity Study in Crl:CD-1(ICR) Mice, 041045.SPT, MRID: N/A, DACO: 4.3.1

1096437 2006, One Year Oral Toxicity - Dog, N/A, MRID: N/A, DACO: 4.3.2

1096438 2005, XDE-175: 90-Day Dietary Toxicity Study in Beagle Dogs, 041114, MRID: N/A, DACO: 4.3.2

1096440 2005, Study Profile Template (SPT) for XDE-175: 90-Day Dietary Toxicity Study in Beagle Dogs, 041114.SPT, MRID: N/A, DACO: 4.3.2

1096441 2004, XDE-175: 28-Day Dietary Toxicity Study in Beagle Dogs, 041028, MRID: N/A, DACO: 4.3.3

1096442 2005, Study Profile Template (SPT) for XDE-175: 28-Day Dietary Toxicity Study in Beagle Dogs, 041028.SPT, MRID: N/A, DACO: 4.3.3

1096443 2004, X574175: 28-Day Dietary Toxicity Study in Fischer 344 Rats, 031151, MRID: N/A, DACO: 4.3.3

1096444 2005, Study Profile Template (SPT) for X574175: 28-Day Dietary Toxicity Study in Fischer 344 Rats, 031151.SPT, MRID: N/A, DACO: 4.3.3

1096445 2005, Report Revision for X574175: 28-Day Dietary Toxicity Study in CD-1 Mice, 031081R, MRID: N/A, DACO: 4.3.3

1096446 2005, Study Profile Template (SPT) for X574175: 28-Day Dietary Toxicity Study in CD-1 Mice, 031081.SPT, MRID: N/A, DACO: 4.3.3

1096447 2005, XDE-175: 28-Day Dermal Toxicity Study in F344/DuCrl Rats, 051052, MRID: N/A, DACO: 4.3.5

1096448 2005, Study Profile Template (SPT) for XDE-175: 28-Day Dermal Toxicity Study in F344/DuCrl Rats, 051052.SPT, MRID: N/A, DACO: 4.3.5

1096449 2007, Chronic Rodent (Species 1) - Rat, N/A, MRID: N/A, DACO: 4.4.1

1096450 2007, Oncogenicity (Rodent Species 1) - Rat, N/A, MRID: N/A, DACO: 4.4.2

1096451 2007, Oncogenicity (Rodent Species 2), N/A, MRID: N/A, DACO: 4.4.3

1096452 2007, Combined Chronic/Oncogenicity (Rodent) - Rat, N/A, MRID: N/A, DACO: 4.4.4

1096453 2006, Multigenerational Reproduction (Rodent), N/A, MRID: N/A, DACO: 4.5.1

1096454 2005, XDE-175: Oral Gavage Developmental Toxicity Probe Study in CRL:CD Rats, 041162, MRID: N/A, DACO: 4.5.2

1096455 2005, XDE-175: Oral Gavage Developmental Toxicity Study in CD Rats, 051033, MRID: N/A, DACO: 4.5.2

1096456 2005, Study Profile Template (SPT) for XDE-175: Oral Gavage Developmental Toxicity Study in CD Rats, 051033.SPT, MRID: N/A, DACO: 4.5.2

1096457 2005, XDE-175: Developmental Toxicity Probe Study in New Zealand White Rabbits, 041062, MRID: N/A, DACO: 4.5.3

1096458 2005, XDE-175: Oral Gavage Developmental Toxicity Study in New Zealand White Rabbits, 041125, MRID: N/A, DACO: 4.5.3

1096459 2005, Study Profile Template (SPT) for XDE-175: Oral Gavage Developmental Toxicity Study in New Zealand White Rabbits, 041125.SPT, MRID: N/A, DACO: 4.5.3

1096460 2005, Salmonella-Escherichia coli/Mammalian-Microsome Reverse Mutation Assay Preincubation Method with a Confirmatory Assay with XDE-175, 6736-150, MRID: N/A, DACO: 4.5.4

1096461 2005, Salmonella-Escherichia coli/Mammalian-Microsome Reverse Mutation Assay Preincubation Method with a Confirmatory Assay with XDE-175, 6736-150, MRID: N/A, DACO: 4.5.4

1096462 2005, Evaluation of XDE-175 in the Chinese Hamster Ovary Cell/Hypoxathine-Guanine-Phosphoribosyl Transferase (CHO/HGPRT) Forward Mutation Assay, 051027, MRID: N/A, DACO: 4.5.5

1096463 2005, Study Profile Template (SPT) for Evaluation of XDE-175 in the Chinese Hamster Ovary Cell/Hypoxathine-Guanine-Phosphoribosyl Transferase (CHO/HGPRT) Forward Mutation Assay, 051027.SPT, MRID: N/A, DACO: 4.5.5

1096464 2005, Evaluation of XDE-175 in an in Vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes, 051026, MRID: N/A, DACO: 4.5.6

1096465 2005, Study Profile Template (SPT) for Evaluation of XDE-175 in an in Vitro Chromosomal Aberration Assay Utilizing Rat Lymphocytes, 051026.SPT, MRID: N/A, DACO: 4.5.6

1096466 2005, Evaluation of XDE-175 in the Mouse Bone Marrow Micronucleus Test, 051034, MRID: N/A, DACO: 4.5.7

1096467 2005, Study Profile Template (SPT) for Evaluation of XDE-175 in the Mouse Bone Marrow Micronucleus Test, 051034.SPT, MRID: N/A, DACO: 4.5.7

1096468 2005, Revised Report for: X517131 (XDE-175 Factor J): Pharmacokinetics and Metabolism in F/344DUCRL Rats, 041137, MRID: N/A, DACO: 4.5.9

1096469 2005, Study Profile Template (SPT) for X517131 (XDE-175 Factor J): Pharmacokinetics and Metabolism in F/344DUCRL Rats, 041137.SPT, MRID: N/A, DACO: 4.5.9

1096470 2005, X513999 (XDE-175 Factor L): Pharmacokinetics and Metabolism in F/344DUCRL Rats, 041138, MRID: N/A, DACO: 4.5.9

1096471 2005, Study Profile Template (SPT) for X513999 (XDE-175 Factor L): Pharmacokinetics and Metabolism in F/344DUCRL Rats, 041138.SPT, MRID: N/A, DACO: 4.5.9

1096472 2005, XDE-175: Acute Neurotoxicity Study in F344/DUCRL Rats, 051037, MRID: N/A, DACO: 4.5.12

1096473 2005, Study Profile Template (SPT) for XDE-175: Acute Neurotoxicity Study in F344/DUCRL Rats, 051037.SPT, MRID: N/A, DACO: 4.5.12

1281064 2006, XDE-175: Two Generation Dietary Reproductive Toxicity Study In CD Rats., 041147; 041147/2; 041147/W1; 041147/W2, MRID: N/S, DACO: 4.5.1

1281117 2006, Revised Report For: XDE-175: Local Lymph Node Assay In Balb/cAnNCrL Mice, 051023; 051023R, MRID: N/S, DACO: 4.2.6,4.8

1305983 Ehling, G. et al, 2005, An European inter-laboratory validation of alternative endpoints of the murine local lymph node assay: First Round, N/A, MRID: N/A, DACO: 4.6.6

1305984 Hariya, T., Hatao, M. Ichikawa, H., 1998, Development of a Non-radioactive Endpoint in a Modified Local Lymph Node Assay, N/A, MRID: N/A, DACO: 4.6.6

1305985 Ryan, C.A. et al, 2002, Examination of a vehicle for use with a water soluble material in the murine local lymph node assay, N/A, MRID: N/A, DACO: 4.6.6

1305986 2004, EF-1186 Fungicide (Quinoxyfen 500 SC) and Two Herbicide Formulations: Local Lymph Node Assay in Balb/C Mice, 040021, MRID: N/A, DACO: 4.6.6

1305987 Wollhiser, M.R. et al, 1998, A Combined Murine Local Lymph Node and Irritancy Assay to Predict Sensitization and Irritancy Potential of Chemicals, N/A, MRID: N/A, DACO: 4.6.6

1305988 Woolhiser, M.R. et al, 1999, Comparison of mouse strains using the local Lymph Node Assay, N/A, MRID: N/A, DACO: 4.6.6

1305999 vant Erve, E.H. M., Wijnand, E. et al, 1998, The Vehicle Modulates Cellular and Humoral Responses in Contact Hypersensitivity to Oxazolone, N/A, MRID: N/A, DACO: 4.6.6

1358463 2006, XDE 175: One Year Dietary Toxicity Study in Beagle Dogs, 051072, MRID: N/A, DACO: 4.3.2

1358464 2006, Study Profile Template for XDE -175: One Year Dietary Toxicity Study in Beagle Dogs, 051072.SPT, MRID: N/A, DACO: 4.3.2

1416002 2007, Study Profile Template for XDE-175: Chronic Neurotoxicity Study in F344/DUCRL Rats, 041155, MRID: n/a, DACO: 4.4.1

1424874 2007, Study Profile Template (SPT) for XDE 175: 18 month dietary oncogenicity in Crl:CD1(ICR) Mice, DN0024509, DACO: 4.4.4

1424875 2007, XDE-175: 18-Month Dietary Oncogenicity Study in Crl: CD1(ICR) Mice, 041164, MRID: n/a, DACO: 4.4.4

1441919 2007, XDE-175: Chronic Neurotoxicity Study in F344/DuCrl Rat, 041155N, MRID: 47105901, DACO: 4.4.1,4.5.14

Food Residues

PMRA Document Number	Reference
1096475	2005, Nature of Residue in te Laying Hen Using14C-XDE-175, 204-0765c, MRID: 46695010, DACO: 6.2
1096476	2005, Study Profile Template (SPT) for Nature of Residue in te Laying Hen Using14C-XDE-175, 040087.SPT, MRID: 46695214, DACO: 6.2
1096477	2005, Nature of Residue Study in the Ruminant Using 14C XDE-175, 040088, MRID: 46695011, DACO: 6.2

1096478 2005, Study Profile Template (SPT) for Nature of Residue Study in the Ruminant Using 14C XDE-175, 040088.SPT, MRID: 46695215, DACO: 6.2

1096479 2005, A Nature of the Residue Study with 14C XDE-175 Applied to Apples, 040050, MRID: 46695009, DACO: 6.3

1096480 2005, Study Profile Template (SPT) for A Nature of the Residue Study with 14C XDE-175 Applied to Apples, 040050.SPT, MRID: 46695213, DACO: 6.3

1306003 2005, A Nature of the Residue Study with 14C XDE-175 Applied to Lettuce, 040048, MRID: 46695007, DACO: 6.3

1096482 2005, Study Profile Template (SPT) for A Nature of the Residue Study with 14C XDE-175 Applied to Lettuce, 040048.SPT, MRID: 46695211, DACO: 6.3

1096483 2005, A Nature of the Residue with 14C XDE-175 Applied to Turnips, 040049, MRID: 46695008, DACO: 6.3

1096484 2005, Study Profile Template (SPT) for A Nature of the Residue with 14C XDE-175 Applied to Turnips, 040049.SPT, MRID: 46695212, DACO: 6.3

790422 1998, Spinosad: Magnitude of the Residue on Potato, 06653.97-DOR01, MRID: N/S, DACO: 7.4.1

790425 2000, Spinosad: Magnitude of the Residue on Beet (Garden), 06906.98-NDR02, MRID: N/S, DACO: 7.4.1

790426 2001, Spinosad: Magnitude of the Residue on Radish (Roots), 07360.99-NDR04, MRID: N/S, DACO: 7.4.1

790431 1997, Magnitude of Residues of Spinosad in Leafy Vegetables, N/S, MRID: N/S, DACO: 7.4.1

790432 1996, Magnitude of Spinosad in Head Lettuce, Spinach and Tomatoes--Bridging Study for NAF-85 and NAF-127 Formulations, N/S, MRID: N/S, DACO: 7.4.1

790433 1997, Residues of Spinosad in Brassicas after Application of Tracer Naturalyte Insect Control in Australia, 1996, N/S, MRID: N/S, DACO: 7.4.1

790434 1996, Magnitude of Residues of Spinosad in Brassica Vegetables, N/S, MRID: N/S, DACO: 7.4.1

790436 1998, Magnitude of Residues of Spinosad in Legumes, N/S, MRID: N/S, DACO: 7.4.1

790439 2001, Spinosad: Magnitude of the Residue on Pea (Dry), 07273.99-NDR03, MRID: N/S, DACO: 7.4.1

790482 1996, Magnitude of Residues of Spinosad in Tomatoes and Peppers, N/S, MRID: N/S, DACO: 7.4.1

790484 1998, Magnitude of Residue of Spinosad in Cucurbit Vegetables, N/S, MRID: N/S, DACO: 7.4.1

790487 1997, Magnitude of Residues in Citrus Fruit and Processed Products After Use of NAF-85 Insecticide, N/S, MRID: N/S, DACO: 7.4.1,7.4.5

790491 2000, Spinosad: Magnitude of the Residue on Pear, 06714.97-DOR02, MRID: N/S, DACO: 7.4.1

790494 1998, Magnitude of Residue of Spinosad in Stone Fruit, N/S, MRID: N/S, DACO: 7.4.1

790495 2001, Spinosad: Magnitude of the Residue on Blueberry, 06850.98-NDR03, MRID: N/S, DACO: 7.4.1

790497 1998, Magnitude of Residues of Spinosad in the Cereal Grains Crop Group (Sweet Corn, Field Corn, Sorghum and Wheat), N/S, MRID: N/S, DACO: 7.4.1

790526 2000, Spinosad: Magnitude of the Residue on Cranberry, 06823.98-NDR04, MRID: N/S, DACO: 7.4.1

790533 1996, Magnitude of Residue of Spinosad in Processed Products of Tomatoes, N/S, MRID: N/S, DACO: 7.4.5

790537 2001, Spinosad: Magnitude of the Residue on Strawberry, 06822.98-NDR05, MRID: N/S, DACO: 7.4.1

1073968 Spinosad: magnitude of the residue on grape, IR-4, GLP, unpublished. 249 pages., DACO: 7.2.1,7.3,7.4.1,7.4.5

1096495 2005, Independent Laboratory Validation of Dow AgroSciences LLC Method GRM 05.15 - Determination of Residues of XDE-175 and its Metabolites in Bovine and Poultry Tissues by High Performance Liquid Chromatography with Tandem Mass Spectrometry, 050049, MRID 46695014, DACO: 7.2.3

1096497 2005, Method Validation Study for the Determination of Residues of XDE-175 and it Metabolites in Bovine and Poultry Tissues, Milk, Cream, and Eggs by Liquid Chromatography with Tandem Mass Spectrometry, 051022, MRID: N/A, DACO: 7.2.2,8.2.2.4

1096498 2005, Study Profile Template (SPT) for the Method Validation Study for the Determination of Residues of XDE-175 and it Metabolites in Bovine and Poultry Tissues, Milk, Cream, and Eggs using Dow AgroSciences Method GRM 05.15, 051022.SPT, MRID: N/A, DACO: 7

1096650 2005, Proposal for Canadian Maximum Residue Limits for XDE-175 treated commodities - GF 1587, N/A, MRID: N/A, DACO: 7.1

1096651 2005, XDE-175 in or on Crops and Livestock: Sections E, F, and G of the Petition for Permanent Tolerances, GH-C 5822, MRID: N/A, DACO: 7.1,7.8

1096652 2005, Method Validation Report for the Determination of Residues of Spinosad and its Metabolites in Agricultural Commodities Using Dow AgroSciences Method GRM 05.14, 040107, MRID: N/A, DACO: 7.2.1,7.2.5

1096653 2005, Study Profile Template (SPT) for the Method Validation Report for the Determination of Residues of Spinosad and its Metabolites in Agricultural Commodities Using Dow AgroSciences Method GRM 05.14, 040107.SPT, MRID: N/A, DACO: 7.2.1,7.2.3

1096654 2005, Method Validation Report for the Determination of XDE-175 and its Metabolites in Agricultural Commodities using Dow AgroSciences Methods GRM 05.03 and GRM 05.04, 041021, MRID: N/A, DACO: 7.2.1,7.2.5

1096655 2005, Study Profile Template (SPT) for the Method Validation Report for the Determination of XDE-175 and its Metabolites in Agricultural Commodities using Dow AgroSciences Methods GRM 05.03 and GRM 05.04, 041021, MRID: N/A, DACO: 7.2.1,7.2.5

1096656 2005, Method Validation Study for the Determination of Residues of XDE-175 and its Metabolites in Bovine and Poultry Tisues, Milk, Cream and Eggs by Liquid Chromatography with Tandem Mass Spectrometry, 051022, MRID: N/A, DACO: 7.2.2

1096657 2005, Study Profile Template for Method Validation Study for the Determination of Residues of XDE-175 and its Metabolites in Bovine and Poultry Tisues, Milk, Cream and Eggs by Liquid Chromatography with Tandem Mass Spectrometry, 051022.SPT, MRID: N/A, DAC

1096658 2005, Independent Laboratory Validation of Dow AgroSciences LLC Method GRM 05.03 - Determination of Residues of XDE-175 and its Metabolites in Agricultural Commodities by Liquid Chromatography with Tandem Mass Spectrometry, P 863 G, MRID: N/A, DACO: 7.2.3

1096660 2005, PAM I Multiresidue Protocol Testing for XDE-175-J, XDE-175-L and their Metabolites N-demethyl-175-J, N-demethyl-175-L, N-formyl-175-J and N-formyl-175-L, 1583, MRID: N/A, DACO: 7.2.4

1096661 2005, Study Profile Template (SPT) for PAM I Multiresidue Protocol Testing for XDE-175-J, XDE-175-L and their Metabolites N-dimethyl-175-J, N-dimethyl-175-L, N-formyl-175-J and N-formyl-175-L, 01583, MRID: N/A, DACO: 7.2.4

1096662 2005, Frozen Storage Stability of XDR-175 and Metabolites in Soil - Interim Report, 050011, MRID: N/A, DACO: 7.3

1096663 2005, Study Profile Template (SPT) for Frozen Storage Stability of XDR-175 and Metabolites in Soil - Interim Report, 050011, MRID: N/A, DACO: 7.3

1096664 2005, Frozen Storage Stability of XDE-175 and Relevant Metabolites in Agricultural Commodities, 050027, MRID: N/A, DACO: 7.3

1096665 2005, Study Profile Template (SPT) for Frozen Storage Stability of XDE-175 and Relevant Metabolites in Agricultural Commodities, 050027.SPT, MRID: N/A, DACO: 7.3

1096666 2005, Magnitude of Residues of XDE-175 and Spinosad in Apples, Leaf Lettuce, Oranges, Sugar Beets and Tomatoes, 040063, MRID: N/A, DACO: 7.4.1,7.4.2

1096666 2005, Magnitude of Residues of XDE-175 and Spinosad in Apples, Leaf Lettuce, Oranges, Sugar Beets and Tomatoes, 040063, MRID: N/A, DACO: 7.4.2

1096667 2005, Study Profile Template (SPT) for Magnitude of Residues of XDE-175 and Spinosad in Apples, Leaf Lettuce, Oranges, Sugar Beets and Tomatoes, 040063.SPT, MRID: N/A, DACO: 7.4.1,7.4.2

1096680 2005, Supervised Residue Trial Study, N/A, MRID: N/A, DACO: 7.4.1

1096681 2005, A Confined Rotational Crop Study with 14C-XDE-175 - Interim Report - The 30-Day Plant-Back Interval, 040086, MRID: N/A, DACO: 7.4.3

1096682 2005, Study Profile Template (SPT) for A Confined Rotational Crop Study with 14C-XDE-175 - Interim Report - The 30-Day Plant-Back Interval, 040086.SPT, MRID: N/A, DACO: 7.4.3

1096683 2005, Livestock, Poultry, Egg, and Milk Residue Data (from feeding treated crops) - GF-1587, N/A, MRID: N/A, DACO: 7.5.1

1173030 MAGNITUDE OF RESIDUE OF SPINOSAD (DE-105) IN APPLES, BRASSICA VEGETABLES, TOMATOES & PEPPERS, HEAD LETTUCE, SPINACH & TOMATOES-BRIDGING STUDY FOR NAF-85 & NAF-127 FORMULATIONS, E.M. BARGAR, H.G. BOLLES, ET AL, 96.05.30 (RES95014;171-4(K);RES95001;RES95

1178531 NAF-85: MAGNITUDE OF RESIDUE OF SPINOSAD (DE-105) IN APPLES, REPORT, E.M. BARGAR, H.G. BOLLES, C.K. ROBB, STUDY COMPLETED MAY 30, 1996 (RES95014) [NAF-85;SUBN.#97-0777;SUBMITTED APRIL 15, 1997;VOLUME 2 METABOLISM], DACO: 7.4.2

1178534 NAF-85: MAGNITUDE OF RESIDUES OF SPINOSAD IN BRASSICA VEGETABLES, REPORT, B.S. RUTHERFORD, G.A. BORMETT, STUDY COMPLETED JUNE 3, 1996 (RES95001) [NAF-85;SUBN.#97-0777;SUBMITTED APRIL 15, 1997;VOLUME 2 METABOLISM], DACO: 7.4.2

1178734 NAF-85: MAGNITUDE OF RESIDUES OF SPINOSAD IN TOMATOES AND PEPPERS, REPORT, B.S. RUTHERFORD, C.K. ROBB, STUDY COMPLETED SEPTEMBER 3, 1996 (RES95016) [NAF-85;SUBN.#97-0777;SUBMITTED APRIL 15, 1997;VOLUME 3 RESIDUES], DACO: 7.4.2

1178745 NAF-85: MAGNITUDE OF RESIDUES OF SPINOSAD IN HEAD LETTUCE, SPINACH AND TOMATOES-BRIDGING STUDY FOR NAF-85 AND NAF-127 FORMULATIONS, REPORT, B.S. RUTHERFORD, A.M. PHILLIPS, C.K. ROBB, STUDY COMPLETED SEPTEMBER 3, 1996 (RES96009;RES96008) [NAF-85;SUBN.#97

1178767 NAF-85: MAGNITUDE OF RESIDUE OF SPINOSAD IN PROCESSED PRODUCTS OF APPLES, REPORT, H.G. BOLLES, C.K. ROBB, STUDY COMPLETED MAY 6, 1996 (RES95041) [NAF-85;SUBN.#97-0777;SUBMITTED APRIL 15, 1997;VOLUME 4 RESIDUES], DACO: 7.4.5

1263510 1998, Spinosad Residues in Potatoes (1997), DACO: 7.4.1

1263511 1998, Temporal Residue Trial Study, DACO: 7.4.2

1281119 2006, Magnitude of the Residue of XDE-175 in Apples, 050041, MRID: N/S, DACO: 7.4.1

1320697 2006, Frozen Storage Stability of XDE-175 and Relevant Metabolites in Agricultural Commodities, 050027.01, MRID: N/A, DACO: 7.3

1320698 2006, Frozen Storage Stability of XDE-175 and Relevant Metabolites in Agricultural Commodities SPT, SPT for 050027.01, MRID: N/A, DACO: 7.3

1320699 2006, Frozen Storage Stability of XDE-175 and Metabolites in Soil, 050011.01, MRID: N/A, DACO: 7.3

1320724 2006, Frozen Storage Stability of XDE-175 and Relevant Metabolites in Agricultural Commodities, 050027.01, MRID: N/A, DACO: 7.3

1320725 2006, Frozen Storage Stability of XDE-175 and Metabolites in Soil, N/A, MRID: N/A, DACO: 7.3

1332357 2005, Proposal for Canadian Maximum Residue Limits for XDE-175 treated commodities - GF 1587, N/A, MRID: N/A, DACO: 7.1

1360133 2007, XDE-175 Livestock Feeding Study: Magnitude of Residue in Milk, Muscle, Fat, Liver and Kidney of Lactating Dairy Cattle, 060052, DACO: 7.5

1360134 2007, Study Profile for XDE-175 Livestock Feeding Study; Magnitude of Residue in Milk, Muscle, Fat, Liver and Kidney of Lactating Dairy Cattle, 060052, MRID: n/a, DACO: 7.5

1385793 2007, Method Validation Report for Method GRM 06.08 - Determination of Residues of XDE-175 and its Metabolites in Bovine and Poultry Tissues, Milk, Cream, and Eggs by Liquid Chromatography with Tandem Mass Spectrometry, 061023, MRID: N/A, DACO: 7.5

1402450 Wright, J.P, et al, 2006, XDE-175 in or on Crops and Livestock: Revised Sections E,F, and G of the Petition for Permanent Tolerances, GH-C 5839, DACO: 7.4.5

1402451 2006, TSN104794 Certificate of Analysis for Test/Reference/Control Substances, 060052, DACO: 7.5

3.0 Impact on the Environment

PMRA Document Number	Reference
1096375	2005, Study Profile Template (SPT) for Aqueous Photolysis of XDE-175 in pH Buffer under Xenon Light, 040079.SPT, MRID: N/A, DACO: 8.2.3.3.2
1096376	2005, Aerobic Soil Degradation of XDE-175 in Four US Soils, 040068, MRID: N/A, DACO: 8.2.3.4.2
1096377	2005, Study Profile Template (SPT) for Aerobic Soil Degradation of XDE-175 in Four US Soils, 040068.SPT, MRID: N/A, DACO: 8.2.3.4.2
1096378	2005, Aerobic Aquatic Metabolism of XDE-175-J and XDE-175-L, 040089, MRID: N/A, DACO: 8.2.3.5.4
1096379	2005, Study Profile Template (SPT) for Aerobic Aquatic Metabolism of XDE-175-J and XDE-175-L, 040089.SPT, MRID: N/A, DACO: 8.2.3.5.4
1096380	2005, Anaerobic Aquatic Metabolism of XDRE-175-J and XDE-175-L, 040065, MRID: N/A, DACO: 8.2.3.5.6
1096381	2005, Study Profile Template (SPT) for Anaerobic Aquatic Metabolism of XDRE-175-J and XDE-175-L, 040065.SPT, MRID: N/A, DACO: 8.2.3.5.6
1096382	2005, Laboratory Studies of Mobility: XDE-175 Summary (B), N/A, MRID: N/A, DACO: 8.2.4.1
1096383	2005, Batch Equilibrium Adsorption/Desorption of XDE-175 and N-demethyl XDE-175 on Four US Soils, 050043, MRID: N/A, DACO: 8.2.4.2
1096384	2005, Study Profile Template (SPT) for Batch Equilibrium Adsorption/Desorption of XDE-175 and N-demethyl XDE-175 on Four US Soils, 050043.SPT, MRID: N/A, DACO: 8.2.4.2
1096385	2005, Terrestrial Field Dissipation of XDE-175 in the USA, 040045, MRID: N/A, DACO: 8.3.2
1096386	2005, Terrestrial Field Dissipation of XDE-175 in the USA (Maybe Small or Large Scale), 040045, MRID: N/A, DACO: 8.3.2
1096387	2005, Study Profile Template (SPT) for Terrestrial Field Dissipation of XDE-175 in the USA, 040045.SPT, MRID: N/A, DACO: 8.3.2
1096388	2005, Aquatic Field Dissipation Study of XDE-175, 050014, MRID: N/A, DACO: 8.3.3

1096389 2005, Field Studies of Dissipation/Accumulation (Maybe Small or Large Scale), MRID: N/A, DACO: 8.3.3

1096390 2005, Study Profile Template (SPT) for Aquatic Field Dissipation Study of XDE-175, 050014.SPT, MRID: N/A, DACO: 8.3.3

1096391 2005, Storage, Disposal, and Decontamination: XDE-175 Summary, N/A, MRID: N/A, DACO: 8.4.1

1096485 2005, Environmental Chemistry and Fate: XDE-175 Technical Summary, N/A, MRID: N/A, DACO: 8.1

1096486 2005, Summary of Physiochemical Properties, N/A, MRID: N/A, DACO: 8.2.1

1096488 2005, Method Validation Report for the Determination of XDE-175 and its Metabolites in Soil and Sediment using Dow AgroSciences Methods GRM 05.01 and GRM 05.02, 041020, MRID: N/A, DACO: 8.2.2.1

1096489 2005, Study Profile Template (SPT) for Method Validation Report for the Determination of XDE-175 and its Metabolites in Soil and Sediment using Dow AgroSciences Methods GRM 05.01 and GRM 05.02, 041020, MRID: N/A, DACO: 8.2.2.1

1096490 2005, Independent Laboratory Validation of Dow AgroSciences Method GRM 05.02 - Determination of Residues of XDE-175 and its Metabolites in Soil and Sediment by On-Line Solid Phase Extraction and Liquid Chromatography with Tandem Mass Spectrometry, GHB-P 1

1096491 2005, Refer to 8.2.2.1 TGAI Product Submission; Method Validation Report for the Determination of XDE-175 and its Metabolites in Soil Sediment using Dow AgroSciences Methods GRM 05.01 and GRM 05.02. Study 041020, 050036, MRID: N/A, DACO: 8.2.2.2

1096492 2005, Method Validation Report for the Determination of XDE-175 and its Metabolites in Water Using Dow AgroSciences Method GRM 05.12, 051017, MRID: N/A, DACO: 8.2.2.3

1096493 2005, Method Validation Report for the Determination of XDE-175 and its Metabolites in Water Using Dow AgroSciences Method GRM 05.12, 051017, MRID: N/A, DACO: 8.2.2.3

1096494 2005, Independent Laboratory Validation of Dow AgroSciences LLC Method GRM 05.12 - Determination of Residues of XDE-175 and its Metabolites in Water by Liquid Chromatography with Tandem Mass Spectrometry, P 865 G, MRID: N/A, DACO: 8.2.2.3

1096495 2005, Independent Laboratory Validation of Dow AgroSciences LLC Method GRM 05.15 - Determination of Residues of XDE-175 and its Metabolites in Bovine and Poultry Tissues by High Performance Liquid Chromatography with Tandem Mass Spectrometry, 050049, MRID

1096500 2005, Hydrolysis of XDE-175-J and XDE-175-L, 040108, MRID: N/A, DACO: 8.2.3.2

1096501 2005, Study Profile Template (SPT) for Hydrolysis of XDE-175-J and XDE-175-L, 040108.SPT, MRID: N/A, DACO: 8.2.3.2

1096502 2005, Photodegradation of XDE-175-J and XDE-175-L on Soil, 050023, MRID: N/A, DACO: 8.2.3.3.1

1096503 2005, Study Profile Template (SPT) for Photodegradation of XDE-175-J and XDE-175-L on Soil, 050023.SPT, MRID: N/A, DACO: 8.2.3.3.1

1096504 2005, Aqueous Photolysis of XDE-175 in pH Buffer under Xenon Light, 040079, MRID: N/A, DACO: 8.2.3.3.2

1106842 2005, Scientific Justification to Support a Waiver Request for the Anaerobic Soil (Flooded) 20-30 degrees Celsius on XDE-175, N/A, MRID: N/A, DACO: 8.2.3.4.4

1121278 DACO: 8.2.2

1320719 2006, Frozen Storage Stability of XDE-175 and Metabolites in Soil, 050011.01, MRID: N/A, DACO: 8.6

1320720 2006, Study Profile Template for Frozen Storage Stability of XDE-175 and Metabolites in Sol, 050011.01, MRID: N/A, DACO: 8.6

1385794 2007, Terrestrial Field Dissipation of XDE-175 in Canada, 050016, MRID: N/A, DACO: 8.3.2

1385795 2007, Study Profile Template for Terrestrial Field Dissipation of XDE-175 in Canada, 050016.SPT, MRID: N/A, DACO: 8.3.2

1096394 2005, Non-Target Terrestrial Invertebrates: XDE-175 TGAI Summaries, N/A, MRID: N/A, DACO: 9.2.1

1096395 2005, XDE-175: Acute Toxicity Test with the Earthworm, Eisenia fetida, 49401, MRID: N/A, DACO: 9.2.3.1

1096396 2005, Study Profile Template (SPT) for XDE-175: Acute Toxicity Test with the Earthworm, Eisenia fetida, 49401, MRID: N/A, DACO: 9.2.3.1

1096397 2004, XDE-175: Acute Contact Toxicity Test with the Honeybee, Apis mellifera, 48882, MRID: N/A, DACO: 9.2.4.1

1096398 2005, Study Profile Template (SPT) for XDE-175: Acute Contact Toxicity Test with the Honeybee, Apis mellifera, 040178.SPT, MRID: N/A, DACO: 9.2.4.1

1096399 2004, XDE-175: Acute Oral Toxicity Test with the Honeybee (Apis mellifera), 48881, MRID: N/A, DACO: 9.2.4.2

1096400 2005, Study Profile Template (SPT) for XDE-175: Acute Oral Toxicity Test with the Honeybee (Apis mellifera), 040179.SPT, MRID: N/A, DACO: 9.2.4.2

1096401 2005, Non-Target Freshwater Inverebrates: XDE-175 TGAI Summary, N.A, MRID: N/A, DACO: 9.3.1

1096402 2005, XDE-175: An Acute Toxicity Study with the Daphnid, Daphnia magna, 041081, MRID: N/A, DACO: 9.3.2

1096403 2005, Study Profile Template (SPT) for XDE-175: An Acute Toxicity Study with the Daphnid, Daphnia magna, 041081.SPT, MRID: N/A, DACO: 9.3.2

1096404 2005, XDE-175: Chronic Toxicity Test with the Water Flea, Daphnia magna, Conducted Under Flow-Through Conditions, 49225, MRID: N/A, DACO: 9.3.3

1096405 2005, Study Profile Template (SPT) for XDE-175: Chronic Toxicity Test with the Water Flea, Daphnia magna, Conducted Under Flow-Through Conditions, 49225, MRID: N/A, DACO: 9.3.3

1096406 2005, XDE-175: Chronic Toxicity Test with the Water Flea, Daphnia magna, Exposed Under Static-Renewal Test Conditions, 49864, MRID: N/A, DACO: 9.3.3

1096407 2005, Study Profile Template (SPT) for XDE-175: Chronic Toxicity Test with the Water Flea, Daphnia magna, Exposed Under Static-Renewal Test Conditions, 49864, MRID: N/A, DACO: 9.3.3

1096408 2005, XDE-175: 28-Day Chronic Toxicity Study with the Midge, Chironomus riparius, Using Spiked Sediment in a Sediment-Water Exposure, 051035, MRID: N/A, DACO: 9.3.4

1096409 2005, Study Profile Template (SPT) for XDE-175: 28-Day Chronic Toxicity Study with the Midge, Chironomus riparius, Using Spiked Sediment in a Sediment-Water Exposure, 051035.SPT, MRID: N/A, DACO: 9.3.4

1096410 2005, Non-Target Marine Invertebrates: XDE-175 TGAI Summary, N/A, MRID: N/A, DACO: 9.4.1

1096411 2005, XDE-175: Acute Toxicity to the Mysid Shrimp, Amercamysis bahia, Determined Under Flow-Through Test Conditions, 48883, MRID: N/A, DACO: 9.4.2

1096412 2005, Study Profile Template (SPT) for XDE-175: Acute Toxicity to the Mysid Shrimp, Amercamysis bahia, Determined Under Flow-Through Test Conditions, 48883, MRID: N/A, DACO: 9.4.2

1096413 2005, XDE-175: Effect on New Shell Growth of the Eastern Oyster (Crassostrea virginica), 48884, MRID: N/A, DACO: 9.4.3

1096414 2005, Study Profile Template (SPT) for XDE-175: Effect on New Shell Growth of the Eastern Oyster (Crassostrea virginica), 040175.SPT, MRID: N/A, DACO: 9.4.3

1096415 2005, XDE-175: Life-cycle Toxicity Test of the Saltwater Mysid, Americamysis bahai, Conducted Under Flow-Through Test Conditions, 48885, MRID: N/A, DACO: 9.4.5

1096416 2005, Study Profile Template (SPT) for XDE-175: Life-Cycle Toxicity Test of the Saltwater Mysid, Americamysis bahai, Conducted Under Flow-Through Test Conditions, 48885, MRID: N/A, DACO: 9.4.5

1096417 2005, Fish: XDE-175 TGAI Summary, N/A, MRID: N/A, DACO: 9.5.1

1096418 2005, XDE-175: An Acute Toxicity Study with the Rainbow Trout, Oncorhynchus mykiss, 051066, MRID: N/A, DACO: 9.5.2.1

1096419 2005, Study Profile Template (SPT) for XDE-175: An Acute Toxicity Study with the Rainbow Trout, Oncorhynchus mykiss, 051066, MRID: N/A, DACO: 9.5.2.1

1096420 2005, XDE-175: Flow-Through Acute Toxicity Test with the Bluegill Sunfish, Lepomis macrochirus, 49402, MRID: N/A, DACO: 9.5.2.2

1096421 2005, Study Profile Template (SPT) for XDE-175: Flow-Through Acute Toxicity Test with the Bluegill Sunfish, Lepomis macrochirus, 49402, MRID: N/A, DACO: 9.5.2.2

1096422 2005, XDE-175: Early Life-stage Toxicity Test with the Fathead Minnow, Pimephales promelas, Under Flow-Through Conditions, 49403, MRID: N/A, DACO: 9.5.3.1

1096505 2005, Study Profile Template (SPT) for GF-1640 (XDE-175): Effects on the Seedling Emergence and Vegetative Vigor of Non-Target Terrestrial Plants (Tier I), 49546, MRID: N/A, DACO: 9.8.4

1096506 2005, XDE-175: Growth Inhibition Test with the Freshwater Aquatic Plant, Duckweed, Lemna gibba, 49141, MRID: N/A, DACO: 9.8.5

1096507 2005, Study Profile Template (SPT) for XDE-175: Growth Inhibition Test with the Freshwater Aquatic Plant, Duckweed, Lemna gibba, 040368.SPT, MRID: N/A, DACO: 9.8.5

1096508 2004, XDE-175: Toxicity of Residues on Foliage to the Honeybee, Apis mellifera, 49083, MRID: N/A, DACO: 9.9

1096509 2005, Study Profile Template (SPT) for XDE-175: Toxicity of Residues on Foliage to the Honeybee, Apis mellifera, 040345.SPT, MRID: N/A, DACO: 9.9

1096525 2005, Study Profile Template (SPT) for XDE-175: Early Life-stage Toxicity Test with the Fathead Minnow, Pimephales promelas, Under Flow-Through Conditions, 49403, MRID: N/A, DACO: 9.5.3.1

1096526 2005, XDE-175: Early Life-stage Toxicity Test with the Sheepshead Minnow, Cyprinodon variegatus, Under Flow-Through Conditions, 49404, MRID: N/A, DACO: 9.5.3.1

1096528 2005, Study Profile Template (SPT) for XDE-175: Early Life-stage Toxicity Test with the Sheepshead Minnow, Cyprinodon variegatus, Under Flow-Through Conditions, 49404, MRID: N/A, DACO: 9.5.3.1

1096529 2005, XDE-175: Factor L (XDE-175-L): A Bioconcentration Study with the Rainbow Trout, Oncorhynchus mykiss, 051010, MRID: N/A, DACO: 9.5.6

1096530 2005, XDE-175: Factor J (XDE-175-J): A Bioconcentration Study with the Rainbow Trout, Oncorhynchus mykiss, 051010, MRID: N/A, DACO: 9.5.6

1096531 2005, Study Profile Template (SPT) for XDE-175: Factor J (XDE-175-J): A Bioconcentration Study with the Rainbow Trout, Oncorhynchus mykiss, 051010, MRID: N/A, DACO: 9.5.6

1096532 2005, Study Profile Template (SPT) for XDE-175: Factor L (XDE-175-L): A Bioconcentration Study with the Rainbow Trout, Oncorhynchus mykiss, 051010, MRID: N/A, DACO: 9.5.6

1096533 2005, Wild Birds: XDE-175 TGAI Summary, N/A, MRID: N/A, DACO: 9.6.1

1096534 2005, XDE-175: An Acute Oral Toxicity Study with the Northern Bobwhite, 379-153, MRID: N/A, DACO: 9.6.2.1

1096535 2005, Study Profile Template (SPT) for XDE-175: An Acute Oral Toxicity Study with the Northern Bobwhite, 050003.SPT, MRID: N/A, DACO: 9.6.2.1

1096536 2005, XDE-175: An Acute Oral Toxicity Study with the Mallard, 379-154, MRID: N/A, DACO: 9.6.2.2

1096537 2005, Study Profile Template (SPT) for XDE-175: An Acute Oral Toxicity Study with the Mallard, 050004.SPT, MRID: N/A, DACO: 9.6.2.2

1096538 2005, XDE-175: A Dietary LC50 Study with the Northern Bobwhite, 379-151, MRID: N/A, DACO: 9.6.2.4

1096539 2005, Study Profile Template (SPT) for XDE-175: A Dietary LC50 Study with the Northern Bobwhite, 050005.SPT, MRID: N/A, DACO: 9.6.2.4

1096540 2005, XDE-175: A Dietary LC50 Study with the Mallard, 379-152, MRID: N/A, DACO: 9.6.2.5

1096541 2005, Study Profile Template for XDE-175: A Dietary study with the Mallard, 050006.SPT, MRID: N/A, DACO: 9.6.2.5

1096542 2005, XDE-175: A Reproduction Study with the Northern Bobwhite, 379-148, MRID: N/A, DACO: 9.6.3.1

1096543 2005, Study Profile Template (SPT) for XDE-175: A Reproduction Study with the Northern Bobwhite, 040346.SPT, MRID: N/A, DACO: 9.6.3.1

1096544 2005, XDE-175: A Reproduction Study with the Mallard, 379-149, MRID: N/A, DACO: 9.6.3.2

1096545 2005, Study Profile Template (SPT) for XDE-175: A Reproduction Study with the Mallard, 040347.SPT, MRID: N/A, DACO: 9.6.3.2

1096546 2005, Non-Target Plants: XDE-175 TGAI Summary, N/A, MRID: N/A, DACO: 9.8.1

1096547 2005, XDE-175: Growth Inhibition Test with the Unicellular Green Alga, Pseudokirchneriella subcapitata, 49140, MRID: N/A, DACO: 9.8.2,9.8.3

1096548 2005, Non-Target Plants: Marine Algae, 49140, MRID: N/A, DACO: 9.8.2,9.8.3

1096549 2005, Study Profile Template (SPT) for XDE-175: Growth Inhibition Test with the Unicellular Green Alga, Pseudokirchneriella subcapitata, 040367.SPT, MRID: N/A, DACO: 9.8.2,9.8.3

1096550 2004, XDE-175: Growth Inhibition Test with the Freshwater Diatom, Navicula pelliculosa, 49142, MRID: N/A, DACO: 9.8.2

1096551 2005, Study Profile Template (SPT) for XDE-175: Growth Inhibition Test with the Freshwater Diatom, Navicula pelliculosa, 040369.SPT, MRID: N/A, DACO: 9.8.2

1096552 2004, XDE-175: Growth Inhibition Test with the Freshwater Blue-Green Algae, Anabaena flos-aquae, 49143, MRID: N/A, DACO: 9.8.2

1096553 2005, XDE-175: Growth Inhibition Test with the Freshwater Blue-Green Algae, Anabaena flos-aquae, 040370.SPT, MRID: N/A, DACO: 9.8.2

1096554 2004, XDE-175: Growth Inhibition Test with the Saltwater Diatom, Skeletonema costatum, 49144, MRID: N/A, DACO: 9.8.3

1096555 2005, Study Profile Template (SPT) for XDE-175: Growth Inhibition Test with the Saltwater Diatom, Skeletonema costatum, 040371.SPT, MRID: N/A, DACO: 9.8.3

1096556 2005, GF-1640 (XDE-175): Effects on the Seedling Emergence and Vegetative Vigor of Non-Target Terrestrial Plants (Tier I), 49546, MRID: N/A, DACO: 9.8.4

1306004 2004, 04175 XDE Acute Toxicity Oyster - Raw Data, 48884R, MRID: N/A, DACO: 9.5.6

1330984 2005, Study Profile Template (SPT) for XDE-175: Acute Toxicity Test with the Earthworm, Eisenia fetida, 49401, MRID: N/A, DACO: 9.2.3.1

1336907 2005, Study Profile Template (SPT) for XDE-175: Acute Oral Toxicity Test with the Honeybee (Apis mellifera), 040179.SPT, MRID: N/A, DACO: 9.2.4.2

1337893 2004, XDE-175: Acute Contact Toxicity Test with the Honeybee, Apis mellifera, 48882, MRID: N/A, DACO: 9.2.4.1

1337901 2005, Study Profile Template (SPT) for XDE-175: Acute Contact Toxicity Test with the Honeybee, Apis mellifera, 040178.SPT, MRID: N/A, DACO: 9.2.4.1

1338132 2005, Study Profile Template (SPT) for XDE-175: Early Life-stage Toxicity Test with the Sheepshead Minnow, Cyprinodon variegatus, Under Flow-Through Conditions, 49404, MRID: N/A, DACO: 9.5.3.1

1338405 2005, Study Profile Template (SPT) for XDE-175: Toxicity of Residues on Foliage to the Honeybee, Apis mellifera, 040345.SPT, MRID: N/A, DACO: 9.9

1339370 2005, XDE-175: Growth Inhibition Test with the Freshwater Blue-Green Algae, Anabaena flos-aquae, 040370.SPT, MRID: N/A, DACO: 9.8.2

1339391 DACO: 9.5.3.1

1339636 2005, Study Profile Template (SPT) for XDE-175: Early Life-stage Toxicity Test with the Fathead Minnow, Pimephales promelas, Under Flow-Through Conditions, 49403, MRID: N/A, DACO: 9.5.3.1

1339646 2005, Study Profile Template (SPT) for XDE-175: Early Life-stage Toxicity Test with the Fathead Minnow, Pimephales promelas, Under Flow-Through Conditions, 49403, MRID: N/A, DACO: 9.5.3.1

1339926 2005, Study Profile Template (SPT) for XDE-175: An Acute Oral Toxicity Study with the Mallard, 050004.SPT, MRID: N/A, DACO: 9.6.2.2

1339993 2005, Study Profile Template (SPT) for XDE-175: Life-Cycle Toxicity Test of the Saltwater Mysid, Americamysis bahai, Conducted Under Flow-Through Test Conditions, 48885, MRID: N/A, DACO: 9.4.5

1340006 2005, Study Profile Template (SPT) for XDE-175: A Dietary LC50 Study with the Northern Bobwhite, 050005.SPT, MRID: N/A, DACO: 9.6.2.4

1340639 2005, Study Profile Template (SPT) for XDE-175: Acute Toxicity to the Mysid Shrimp, Amercamysis bahia, Determined Under Flow-Through Test Conditions, 48883, MRID: N/A, DACO: 9.4.2

1340669 2005, XDE-175: Growth Inhibition Test with the Freshwater Blue-Green Algae, Anabaena flos-aquae, 040370.SPT, MRID: N/A, DACO: 9.8.2

1343214 2005, Study Profile Template (SPT) for XDE-175: An Acute Toxicity Study with the Daphnid, Daphnia magna, 041081.SPT, MRID: N/A, DACO: 9.3.2

1343225 2005, Study Profile Template (SPT) for XDE-175: An Acute Toxicity Study with the Rainbow Trout, Oncorhynchus mykiss, 051066, MRID: N/A, DACO: 9.5.2.1

1343387 DACO: 9.8.2-9.8.3-9.8.6

1343453 2005, Study Profile Template (SPT) for XDE-175: A Reproduction Study with the Northern Bobwhite, 040346.SPT, MRID: N/A, DACO: 9.6.3.1

1343455 2005, Study Profile Template (SPT) for XDE-175: A Reproduction Study with the Mallard, 040347.SPT, MRID: N/A, DACO: 9.6.3.2

1343498 2005, Study Profile Template (SPT) for XDE-175: Effect on New Shell Growth of the Eastern Oyster (Crassostrea virginica), 040175.SPT, MRID: N/A, DACO: 9.4.3

1343552 2005, Study Profile Template (SPT) for XDE-175: Growth Inhibition Test with the Saltwater Diatom, Skeletonema costatum, 040371.SPT, MRID: N/A, DACO: 9.8.3

1343553 2005, Study Profile Template (SPT) for GF-1640 (XDE-175): Effects on the Seedling Emergence and Vegetative Vigor of Non-Target Terrestrial Plants (Tier I), 49546, MRID: N/A, DACO: 9.8.4

1343567 2005, Study Profile Template (SPT) for XDE-175: An Acute Oral Toxicity Study with the Northern Bobwhite, 050003.SPT, MRID: N/A, DACO: 9.6.2.1

1343963 2005, Study Profile Template (SPT) for XDE-175: Growth Inhibition Test with the Unicellular Green Alga, Pseudokirchneriella subcapitata, 040367.SPT, MRID: N/A, DACO: 9.8.2,9.8.3

1343996 2005, Study Profile Template (SPT) for XDE-175: Growth Inhibition Test with the Freshwater Diatom, Navicula pelliculosa, 040369.SPT, MRID: N/A, DACO: 9.8.2

1344018 2005, Study Profile Template (SPT) for XDE-175: Chronic Toxicity Test with the Water Flea, Daphnia magna, Exposed Under Static-Renewal Test Conditions, 49864, MRID: N/A, DACO: 9.3.3

1344495 2005, Study Profile Template for XDE-175: A Dietary study with the Mallard, 050006.SPT, MRID: N/A, DACO: 9.6.2.5

1344498 2005, Study Profile Template (SPT) for XDE-175: A Dietary LC50 Study with the Northern Bobwhite, 050005.SPT, MRID: N/A, DACO: 9.6.2.4

1344524 2005, Study Profile Template (SPT) for XDE-175: Early Life-stage Toxicity Test with the Sheepshead Minnow, Cyprinodon variegatus, Under Flow-Through Conditions, 49404, MRID: N/A, DACO: 9.5.3.1

1344862 2005, Study Profile Template (SPT) for XDE-175: Flow-Through Acute Toxicity Test with the Bluegill Sunfish, Lepomis macrochirus, 49402, MRID: N/A, DACO: 9.5.2.2

1345361 2005, Study Profile Template (SPT) for XDE-175: Chronic Toxicity Test with the Water Flea, Daphnia magna, Conducted Under Flow-Through Conditions, 49225, MRID: N/A, DACO: 9.3.3

1345874 2005, Study Profile Template (SPT) for XDE-175: Growth Inhibition Test with the Freshwater Aquatic Plant, Duckweed, Lemna gibba, 040368.SPT, MRID: N/A, DACO: 9.8.5

1347383 2005, Study Profile Template (SPT) for XDE-175: 28-Day Chronic Toxicity Study with the Midge, Chironomus riparius, Using Spiked Sediment in a Sediment-Water Exposure, 051035.SPT, MRID: N/A, DACO: 9.3.4

1178437 1997, Acute toxicity of xde-105 insecticide to the sheepshead minnow, Report, J.J. YURK, completed August 27, 1993 (392302102003140;ES-2540) [Spinosad technical; subn.#97-0754;submitted april 15, 1997; volume 2], DACO: 9.5.2.4.1

1096684 2005, GF-1587 Summaries: Environmental Chemistry and Fate, N/A, MRID: N/A, DACO: 8.1

1096687 2005, Field Studiesof Dissipation Accumulation. XDE-175 Summary, N/A, MRID: N/A, DACO: 8.3.1

1096688 2005, Terrestrial Field Dissipation of XDE-175 in the USA, 040045, MRID: N/A, DACO: 8.3.2

1096689 2005, Study Profile Template (SPT) for Terrestrial Field Dissipation of XDE-175 in the USA, 040045, MRID: N/A, DACO: 8.3.2

1096690 2005, Aquatic Field Dissipation Study of XDE-175, 050014, MRID: N/A, DACO: 8.3.3

1096691 2005, Study Profile Template (SPT) for Aquatic Field Dissipation Study of XDE-175, 050014, MRID: N/A, DACO: 8.3.3

1096692 2005, Storage, Disposal and Decontamination: GF-1587 Summary, N/A, MRID: N/A, DACO: 8.4.1

1096393 2005, Environmental Toxicology: XDE-175 TGAI Summary, N/A, MRID: N/A, DACO: 9.1

1096499 2005, Laboratory Studies of Transformation: XDE-175 Summary, N/A, MRID: N/A, DACO: 8.2.3.1

5.0 Value

PMRA Document Number	Reference
1096707	2005, Small Plot Efficacy Trials - GF-1587, DACO: 10.2.3.3
1360136	2007, Small Scale Trials, DACO: 10.2.3.3(B)
1441925	2007, Part 10 Value, DACO: 10.1, 10.2.1, 10.2.2, 10.2.3, 10.2.3.1, 10.2.3.3, 10.3.1, 10.3.2, 10.4, 10.5.1, 10.5.2, 10.5.3

B. ADDITIONAL INFORMATION CONSIDERED

i) Published Information

3.0 Impact on Human and Animal Health

PMRA #	References
649920	2001, REG2001-10 Spinosad (Success 480SC Naturalyte Insect Control Product, Conserve 480SC Naturalyte Insect Control Product), August 17, 2001
1459073	Lullmann, H, Lullmann-Rauch, R., Wassermann, O, 1975, Drug-Induced Phospholipidoses, CRC Critical Review in Toxicology, pages 185-218, DACO: 11.1
1459077	Reasor, M.J., 1988, A Review of the Biology and Toxicologic Implications of the Induction of Lysosomal Lamellar Bodies by Drugs, Toxicology and Applied Pharmacology, 97, 47-56 (1988), DACO: 11.1
1459080	Halliwell, W.H., 1997, Cationic Amphiphilic Drug-Induced Phospholipidosis, Toxicologic Pathology ISSN: 0192-6233, Volume 25, pages 53-60, DACO: 11.1
1459083	Lullmann, H., Lullmann-Rauch, R., Wassermann, O., Commentary - Lipidosis Induced by Amphiphilic Cationic Drugs, Biochemical Pharmacology, Vol. 27, pp. 1103-1108, DACO: 11.1
1459084	Schneider, P., Drug-induced lysosomal disorders in laboratory animals: new substances acting on lysosomes, Arch. Toxicol. (1992) 66: 23-33, DACO: 11.1
1459085	Reasor, M.J., Kacew, S., Minireview - Drug-Induced Phospholipidosis: Are There Functional Consequences? Society for Experimental Biology and Medicine, pages 825-830, DACO: 11.1